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Chapter 1

INTRODUCTION AND RESEARCH QUESTIONS

General Introduction

Pain as defined by the International Association for the study of Pain (IASP) is *"an unpleasant sensory & emotional experience associated with actual or potential tissue damage or described in terms of tissue* damage".[1] A more recent (2015) definition of chronic pain is given by Treede et al: "Pain is a distressing experience associated with actual or potential tissue damage with sensory, emotional, cognitive and social components. Usually pain is regarded as chronic when it lasts or recurs for more than 3 to 6 months".[2] Chronic pain has a worldwide prevalence of 20 to 40%.[3,4] Chronic pain patients not only experience severe problems with sleeping, functioning and quality of life but also suffer from depression.[5] Chronic pain is not only an unpleasant sensation but also results in sick leave and is accompanied by considerable direct and indirect costs.[6]

In a worldwide study by Vos et al, back and neck pain dominated the "Top ten causes of years lived with disability" for almost every high income nation.[7] This is also the situation in the Netherlands, where chronic low back, shoulder and neck pain and osteoarthritis of the knee have the greatest prevalence.[8] According to the American Association of Pain Medicine, more Americans suffer from chronic pain than of diabetes, heart disease and cancer combined.[9] Even though chronic pain is a serious medical and socioeconomic problem, and can be considered as disease in its own right, no governmental health institutions and scientific societies consider chronic pain or pain in general as a high impact disease.[6] Epidemiological research helps to raise awareness of the extensive problems associated with chronic pain and can direct future research areas to improve pain medicine. For example, Bekkering et al. mentioned that increasing accessibility to adequate treatment for all chronic pain sufferers should reduce the negative consequences of it on individual and public health level and, therefore, chronic pain deserves to get more attention from Dutch healthcare workers and policy makers.[10]

The practice of pain management in the cervical region and the head

Ideally, adequate treatment of pain in the cervical region and the head only can be offered after a comprehensive medical analysis, consisting of medical history taking, physical examination and, if indicated, complementary diagnostic testing resulting in a medical hypothesis and consequently in an appropriate differential diagnosis.[6] Besides detailed medical history taking regarding pain characteristics and the impact of pain on different domains (e.g. physical, psychosocial, function, work, related complaints and comorbidities), other factors such as concomitant symptoms, psychiatric history, previous drug dependency, drug use, previous pain assessments or (the effect of) previous treatments, complemented by a physical examination with focus on neurological and musculoskeletal tests should be taken into account. Additional diagnostics consists of MRI, electrophysiological examination and e.g. a segmental selective diagnostic blockade.

Besides the distinction between acute and chronic pain several other characteristics can classify pain during history and physical examination. Most importantly: (1) the exact location (e.g. which cervical level or what region of the head), (2) specific characteristics (somatic, visceral, referenced pain), (3) the origin of pain (e.g. oncological) and (4) underlying pathophysiology (nociceptive versus neuropathic and mixed). Understanding the origin and characteristics of pain will

help to make a patient centered treatment proposal that fits on patients' needs and wishes. Determining which pain category is present can help with specifying the treatment plan. One must however remember that pain often is multifactorial. The following four categories of chronic pain can be distinguished, namely: (1) Neuropathic pain, both peripherally and centrally; (2) Musculoskeletal pain e.g. cervical pain or myofascial pain; (3) Inflammatory pain (arthritis, infection), and: (4) Mechanical/ compression pain (e.g. visceral pain by tumor pressure).[10] In the interventional pain practice of cervical pain one can find two kinds of vertebral related pain: one with mechanical and one with neurological causes. In the category of mechanic pain there are for example facet syndrome, discogenic pain, atlantoaxial (AA) joint pain, cervical-related neck pain (Whiplash Associated Disorders = WAD).[11] From the neurologic causes there are for example Hernia Nucleus Pulposus, irritation of the cervical peripheral nerve or pathology of the dorsal root ganglion (DRG). One can distinguish two types of pain based on their pathophysiology: nociceptive pain (an appropriate physiological response to a painful stimulus) and neuropathic pain (an inadequate response caused by dysfunction of a part of the nervous system). These two types of pain can occur simultaneously in various disorders and are then referred to as 'mixed' pain. The current management of chronic pain in the cervical region consists of conservative and interventional treatment. Both are mentioned further in this thesis, with special attention for cervical discogenic pain treated with e.g. percutaneous nucleoplasty[12], for cervicogenic pain, headaches and WAD with for example percutaneous radiofrequency/pulsed radiofrequency (RF/PRF) of the facet joint (zygapophyseal), of the AA joint[13], for cervical disc hernia with PRF of cervical DRG and for facial pain as Trigeminal Neuralgia with RF/PRF of ganglion of gasser.[14]

Table 1, Treatment possibilities for chronic pain in the cervical region		
Conservative	- Physiotherapy - Trans Electric Nerve Stimulation - Manual medicine - Neurofeedback	Advice: Repeat treatment if patient responds well
Pharmacological	- Non-steroidal anti-inflammatory agents	Advice: Cox-2 inhibitors are preferred above Cox-1 due to less side effects
	- Tricyclic antidepressants - Anti neuropathica - Anti epileptica - Benzodiazepines - Carbamazepine - Oxacarbamazepine - Opiates	Advice: With attendance of neuropathic pain the combination of three medications can be considered, (Anti consulvants, Anti Depressiva and Opiates).
Interventional	- Epidural corticosteroid administration	Advice: Epidural treatment only for subacute HNP
	- (Pulsed) radiofrequency treatment - Percutaneous Cervical Nucleoplasty - Surgery	Advice: RF lesion for facet pain. PRF for DRG of the AA joint. For PCN the disc height should be 50% of normal and should not be used in case of a 'black disc'.

In clinical practice, multidisciplinary rehabilitation with behavioral therapy is recommended.

The principle of epidural administration of corticosteroids is based on the anti-inflammatory effect by inhibition of the phospholipase A2-arachidonic acid cascade-initiated. There are several approaches: the interlaminar and transforaminal way, but at the cervical level no direct comparative outcome studies are published. There is evidence for pain relief after interlaminar administration but the transforaminal administration was more commonly used because of the more precise delivery at the level of the inflamed nerve root.[15] However, several cases with serious neurological complications using the transforaminal route, some with fatal outcome, are reported in literature.[16,17] Based on these findings there is now more support for the interlaminar route.[18] A stepped care approach (Table 1) for the treatment of cervical pain is commonly used with surgery only indicated for the most severe and therapy resistant cases if a neurological deficit is present resulting in motor dysfunction.

Minimally invasive techniques for treating head and neck pain

The extensive observational descriptions of the positive effects of Radiofrequency (RF) treatment in clinical diagnosis of chronic degenerative cervical facet pain resulted in percutaneous facet denervation (PFD) being an accepted treatment option. RF is nowadays still applied for various pain conditions such as tumor pain, nerve pain including trigeminal neuralgia and soft tissue stenosis.[19-21] Afterwards Pulsed Radiofrequency (PRF) treatment was discovered for different indications such as radicular pain, trigeminal neuralgia (TN), occipital neuralgia, shoulder and knee pain.[22] The first PRF procedure on a lumbar dorsal root ganglion was done in 1996.[23-25] Following this experience many kinds of chronic pain were treated successfully with PRF, including cervicobrachial pain, facial pain including trigeminal neuralgia (TN), sacroiliac joint pain, facet pain, shoulder pain, postsurgical pain, radicular pain, groin pain and myofascial pain conditions.[26]

Specific techniques for cervical radicular pain

Percutaneous Cervical Nucleoplasty

Cervical discogenic pain is often caused by cervical disc pathology and hence results in suffering and disability in the adult population.[27] In general it is a difficult and costly health care issue.[28] Approximately 1 person in 1,000 suffers from cervical radicular pain.[29,30] Treatment options range from conservative to surgical interventions.[31] Pain management for cervical disc herniation relies initially on conservative care (rest, physiotherapy, and oral medications). Once conservative treatment has failed, different percutaneous minimally invasive (radiological) procedures can be applied to relief pain.[27] These procedures mainly aim at relieving compression or chemical irritation on sensory structures while minimizing trauma to normal tissues and enhancing patient recovery.[32,33] Although many treatment modalities are described in the literature, the available evidence for efficacy is not sufficient to allow definitive conclusions on the optimal therapy to be made.[29,31] The basic principle of most percutaneous procedures is that a small reduction of volume in a hydraulic space, like an intact disc, results in a disproportionately large fall in pressure. Removal of approximately 1 mL of disc tissue volume, corresponds to a discal volume reduction of about 10-20%[33,34] resulting in a relief of some chemical and mechanical factors causing pain.[27] While the basic mechanism of percutaneous disc decompression (PDD) has been well understood, each method has its own limitations like removal of too much tissue, indiscriminate removal of tissue, thermal injury to the disc or aggressive access into the disc.[35,36] A variety of published studies have demonstrated percutaneous cervical nucleoplasty (PCN) to be both safe and effective in experienced hands.[27,32,35-37] PCN is the most often applied technique on the cervical level with a low risk of thermal damage.[27]

Pulsed radiofrequency of the dorsal root ganglion

PRF of the dorsal root ganglion is well known pain treatment modality and is used as a non- or minimally neuromodulatory technique, and full alternative to radiofrequency heat lesions which can be neuro-ablative.[12] The application of pulsed radiofrequency shows a significant reduction in complications or side effects

compared to radiofrequency techniques.[38] PRF treatment is also indicated at the spinal ganglion for chronic cervical radicular pain.[39,40] More recent studies showed that PRF procedures are probably more effective than conventional radiofrequency in the treatment of chronic pain.[41,42] Besides being more effective, PRF has also a significant reduction in complications or side effects compared to conventional radiofrequency.[43] This opened the possibility to apply PRF treatment for peripheral neuropathies, arthrogenic pain, painful trigger points and neuropathy or radiculopathy by application in dorsal root ganglion.[44] Both techniques are applied in clinical practice with promising results, however evidence for the effectiveness of these interventions is not yet well documented.[32] There is a need for more high-quality RCTs investigating the efficacy and safety of both techniques using validated outcome measures.[31,36,37] Moreover, cost-effectiveness concerning these treatments of cervical discogenic pain should be analyzed.

Surgical treatment

Surgery is indicated for cervical radiculopathy with spinal cord compression and possible injury, which if left untreated can lead to progressive and potentially irreversible neurological deficits. Surgical treatment may give pain relief in patients whose symptoms turn out to be resistant to all other treatments. In a randomized study comparing surgical treatment with conservative treatment, three months after the intervention a significantly better pain relief with surgery was demonstrated. However, one year after surgery, there was no difference between the two groups.[45] In conclusion, there is no gold standard in the treatment of cervical radicular pain. History taking and physical examination are the cornerstones of the diagnostic process. Medical imaging, with a preference for MRI, is indicated for suspected specific pathology and/or neurological symptoms.

PRF in Trigeminal Neuralgia

The effectiveness of PRF for the treatment of trigeminus neuralgia was debated in several publications.[46,47] But in the study by van Zundert et al. and by Yao et al., PRF proved to be successful for treating this condition.[48,49] Therefore we should consider using PRF as an alternative method in trigeminal neuralgia especially in patients with anesthesia dolorosa, for very old patients and in doubtful cases, taking in account that in our experience over the past years practically no side effects of PRF were observed.

Aim of the thesis and research questions:

The aim of this thesis is to investigate the clinical effectiveness and safety of minimal invasive interventional techniques in patients with head and neck pain. This has led to the following research questions for this thesis:

1. Is pulsed radiofrequency application of the antero-lateral C1-2 a safe and effective technique in patients with cervicogenic headaches who are non-responsive to conservative treatment such as medication, physiotherapy, manipulation, mobilization and to other techniques such as intra-articular steroid injections, medial branch of lower cervical blocks and epidural injections?
2. Is there evidence for the use of pulsed radiofrequency application of C1-2 in whiplash patients?
3. Is pulsed radiofrequency treatment also effective in trigeminal neuralgia?
4. Is percutaneous cervical nucleoplasty for patients with a symptomatic disc hernia, a safe and effective method to treat patients?
5. What is the clinical effectiveness of pulsed radiofrequency compared to percutaneous cervical nucleoplasty in cervical disc hernia?

Outline of this thesis

In chapter 2 we retrospectively review the effects of lateral C1-2 joint pulsed radiofrequency treatment in patients who suffer from cervicogenic headache. In chapter 3 we review patients who have whiplash symptoms including cervicogenic headache and who are treated with an antero-lateral atlantoaxial joint pulsed radiofrequency procedure. In chapter 4 we report the results for a cohort of consecutive patients who underwent pulsed radiofrequency treatment for trigeminal neuralgia. Chapter 5 describes the long-term efficacy and safety of percutaneous cervical nucleoplasty in patients with a contained herniated disc. In chapter 6 we systematically review current evidence for percutaneous nucleoplasty as a treatment for patients who suffer from a cervical herniated disc. Chapter 7 reports on a prospective, randomized controlled trial comparing percutaneous cervical nucleoplasty against pulsed radiofrequency of the dorsal root ganglion in patients with a contained cervical disc herniation. Chapter 8 summarizes the presented study results and synthesizes the conclusions of this thesis, including directions for future clinical practice and research.

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Chapter 2

Long-Term Pain Relief in Patients with Cervicogenic Headaches after Pulsed Radiofrequency Application into the Lateral Atlantoaxial (C1-2) Joint Using an Anterolateral Approach

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Abstract

The lateral atlantoaxial joint has long been reported as a source of cervicogenic headache. We present a retrospective study, including 86 patients who had undergone lateral C1-2 joint pulsed radiofrequency application, for cervicogenic headache in a single pain center from March 2007 to December 2008. The percentage of patients who had ≥50% pain relief at 2 months, 6 months, and 1 year were 50% (43/86), 50% (43/86), and 44.2% (38/86), respectively. Longterm pain relief at 6 months and 1 year were predicted reliably by ≥ 50% pain relief at 2 months ($P < 0.001$). Apart from 1 patient that complained of increased severity of occipital headache lasting several hours, we had no other reported complications.

Introduction

The C2 spinal nerve and its dorsal root ganglion have a close proximity to the lateral capsule of the atlantoaxial (C1-2) zygapophyseal joint, and its branches innervate both the C1-2 and C2-3 zygapophyseal joints. Hence, pathologic, inflammatory, and traumatic changes around these joints can be a source of referred head pain. The pars caudalis of the spinal nucleus of the trigeminal nerve is continuous longitudinally with the outer laminae (laminae I-V) of the dorsal horns of the upper 3 to 4 segments of the cervical spinal cord.[1,2] This functional intersection of upper cervical and trigeminal sensory pathways is believed to allow the bidirectional transmission of pain signals between the neck and the trigeminal sensory receptive fields of the face and head. This convergence of afferents from both the trigeminal nerve and the upper 3 cervical spinal nerves provides for the various patterns of referred pain.[3–5]

Clinical presentations that are suggestive of pain originating from the lateral C1-2 joint include: (1) occipital or suboccipital pain, (2) focal tenderness over the suboccipital area or over the transverse process of C1, (3) restricted painful rotation of C1 on C2, and (4) pain provocation by passive rotation of C1.[5] Pain map studies have shown that pain distribution patterns are not indicative of its source or even the joint responsible.[4] At best, these clinical signs have a positive predictive value of only 60%.[4,5] A major diagnostic criterion is the response to a diagnostic intra-articular local anesthetic injection.[4,6] Thereafter, an intra-articular steroid injection can be considered. However, such intra-articular injections are often limited in their duration of efficacy. There has been limited data that lateral C1-2 joint interventions have long-term efficacy despite their establishment as a possible source of pain generation in cervicogenic headaches.[5] In fact, much work has been initiated to find an alternative for intra-articular steroid injections with a longer duration of pain relief.[7]

Even though there is good evidence that the lateral atlantoaxial joint is a source of cervicogenic headache,[8] to our knowledge, there are currently no published studies that have examined the long-term efficacy of lateral atlantoaxial pulsed radiofrequency (PRF) application using the anterolateral approach. We now describe a retrospective study in 86 patients, many of which had suffered from severe headache for more than 10 years in duration.

Methods

Institutional research review board approval was obtained prior to the retrospective collection of data from all 86 patients. This retrospective study included all 86 patients who had undergone lateral C1-2 joint PRF application for cervicogenic headache, in a single pain center from March 2007 to December 2008. The data were collected from the review of patients' medical records, pain questionnaires, and telecommunication verification of details that were not available on the records. From the retrospective data, it was found that all patients were predominantly more disturbed by the headaches than by their accompanying neck pain. However, apart from a predominant unilateral nature of the headache and association with ongoing chronic neck pain, a detailed description of the headaches was not available at the time of writing this manuscript. All the therapeutic procedures were done by one investigator, (W.H.) while the phone verification was done by another assistant with no direct involvement in the interventional procedures or the data analysis process. The C1-2 PRF application was performed using the intra-articular anterolateral approach under fluoroscopic guidance. Patients lie comfortably in a supine position, with standard monitors in place, and head in slightly extended position. The fluoroscopy C-arm is brought to the head of the table in an anteroposterior direction. Under fluoroscopic guidance, the C-arm is rotated in the sagittal plane until the lateral atlantoaxial joint is visualized with its characteristic biconcave appearance. The C-arm is then given an oblique tilt of about 10 to 20 degrees to enhance the imaging of the lateral C1-2 joint as in Figure 1. The needle insertion site is marked, and the skin overlying the lateral aspect of the C1-2 joint is prepped and draped in the usual sterile fashion. After local anesthetic infiltration of the entry point, a 22 G 45mm insulated radiofrequency needle with 5mm active tip is advanced in the posteromedial direction. This approach avoids possible contact and damage to the C2 nerve root and dorsal root ganglion, which is a possible complication from the posterior approach. It is imperative that the lateral C1-2 joint is not approached too laterally to avoid veering into the foramen transvasarium, which may result in vertebral artery puncture.

Figure 1. Oblique view of lateral C1-2 facet joint with needle tip directed toward joint.

Bone is often contacted, which allows estimation of depth. The needle is withdrawn slightly and directed toward the anteromedial portion of the lateral C1-2 joint. A characteristic pop is felt as the joint is entered, usually after advancing only a few millimeters. The anteroposterior view (open mouth view) shows the tip of the needle in lateral 1/3 of the lateral C1-2 joint as seen in Figure 2. A lateral check view shows the tip of the needle in the middle of the joint posterior to the anterior margin of the joint. In our center, we do not routinely give contrast to delineate the joint and hence we avoid the joint distension pain or discomfort that has been described with lateral C1-2 joint injections. It is also for this reason that we do not routinely perform diagnostic injections in the lateral C1-2 joint, which in our experience can even result in transient ataxia.

However, prior to PRF application, sensory stimulation at 50 Hz up to 1.0 V confirms the intra-articular position of the active tip. Motor stimulation at 2 Hz up to 1.0 V is expected to be negative. PRF application is then initiated at 45 V, 2 Hz, and 10 ms for 10 minutes after positive sensory stimulation.[7] No local anesthetic or steroid solution is given after the PRF application.

All patients were followed up with a telephone consultation after 2 weeks to exclude any major complications. Responders were defined as having more than 50% pain relief after the procedure as per the routine clinical practice in this center. All the patients were followed up at 2-month and 6-month intervals in the clinic. Patients were also contacted by telephone at the 1-year interval to determine their response.

Data were recorded on a Microsoft® Excel 97 (Microsoft Corporation, Redmond, WA). The SPSS version 16.0 Statistical Package (SPSS Inc., Chicago, IL) was used to generate frequency tables. The mean, SD, and 95% confidence intervals were tabulated. Differences in proportions and means were tested using linear regression and results were considered statistically significant if the P value was <0.05.

Results

Eighty-six patients underwent C1-2 injection from March 1, 2007 to December 31, 2008. There was no significant difference in the demographics between responders and nonresponders. The percentage of patients who had ≥ 50% pain relief at 2 months, 6 months, and 1 year were 50% (43/86), 50% (43/86), and 44.2% (38/86), respectively. Long-term pain relief at 6 months and 1 year were predicted reliably by ≥ 50% pain relief at 2 months ($P < 0.001$).

As shown in Table 1, the duration of pain before procedure was 9.4 ± 1.1 years (mean ± SE), while baseline pain score was 8.5 ± 0.1. Both these variables were nonsignificant predictors of ≥ 50% pain relief at 2 months, 6 months, and 1 year ($P > 0.05$). There are 48.8% (42/86) of patients with ongoing insurance claims while 90.7% (78/86) had undergone a previous nonsurgical procedure for similar complaints. Both of these factors were nonsignificant predictors of ≥ 50% pain relief at 2 months, 6 months, and 1 year ($P > 0.05$). Apart from 1 patient that complained of increased severity of occipital headache lasting several hours, we had no other recorded complications. The limitations of this study are those inherent to retrospective studies of such nature where data have been collected in a clinical context and, as an example, did not allow us to quantify the reductions in pain medications over 1 year of follow-up.

Figure 2. Anteroposterior view of lateral C1-2 facet joint with needle tip within lateral 1/3 of joint.

Table 1. Demographic Characteristics

Demographic Characteristics	**n = 86**
Gender	
Male	37% (32/86)
Female	63% (54/86)
Age (years) Mean ± SD	50 ± 2.1
Duration of headache (years) Mean ± SD	9.4 ± 1.1
Visual analog scale before C1-2 pulsed radiofrequency Mean ± SD	8.5 ± 0.1
History of previous percutaneous interventions	90.7% (78/86)
Insurance claims	48.8% (42/86)

Discussion

In this retrospective study, we showed that PRF of the C1-2 joint is a feasible technique resulting in good outcome in patients with headaches without serious or long-term complications in experienced hands.

In 1998, Sluijter et al. applied high-voltage RF current in bursts of 20 ms per 500 ms, permitting the generated heat to be washed out during 480 ms “silent phase.” This idea of applying high-voltage energy near a nerve without subsequent heat-induced nerve injury was later termed pulsed radiofrequency (PRF). Since then, it has become clear that at tip temperatures below 45°C, neuronal destruction as a result of permanent heat-induced ultrastructural damages do not usually occur. However, morphological changes such as endoplasmic reticulum cisterns enlargement and increase in the numbers of vacuoles are observed under electron microscopy after PRF have been reported.[9] The mechanism of action of PRF application (though not entirely clear) may possibly be via a combination of excitatory C-fiber response suppression (as evidenced by the extended duration of c-FOS expression) as well as inhibition of synaptic transmission with the decrease in excitatory postsynaptic potential.[2,10,11] This long-term depression of the first synapse, as a result of the generated electric fields within the small joint, most likely explains the immediate effects of the lateral C1-2 joint PRF application. In addition, intra-articular PRF produces an effect of a more gradual onset that is not strictly bound to the strength of the electric field at increased distance from the electrode. This could possibly reflect an action of electric fields on immune cells that influences the production of anti-inflammatory cytokines. The production of proinflammatory cytokines such as interleukin (IL)-1b, tumor necrosis factor a, and IL-6 is likely to be attenuated by the generated electric fields.[7,12]

The lateral atlantoaxial joints are laterally very narrow and a true lateral approach is not feasible. However, when the needle is introduced percutaneously just posterior and caudal to the mandibular angle, and directed slightly cranially and posteriorly, it can easily be advanced into the wider anterior portion of the lateral joint.[13] Such an anterolateral approach is believed to reduce the incidence of C2 nerve root injury, dura cuff puncture, epidural injection, and vertebral artery puncture. In addition, as no local anesthetic or steroid solution is injected, the incidence of ataxia and inadvertent vascular injection is minimal.

In a recent anatomical study, terminal branches of both the superficial and deep cervical prevertebral plexus were seen to attach firmly to the lateral C1-2 joint capsule. It is most likely that the lateral C1-2 joint receives ventral innervation from these nerves. The superficial cervical prevertebral plexus is located deep to the longus capitis muscle and ventral to the anterior tubercles of the cervical transverse process and intervertebral foramina. It is composed of branches from

the C1-3 ventral rami and consists of numerous interconnecting arcades. The deep cervical prevertebral plexus is located deep to the longus cervicis muscle and within the periosteum of the C2 vertebral body in its ventral gutter. It is formed from branches of the ventral rami of C3 and sometimes C4.[14] This is also a likely explanation for the success of the anterolateral approach to lateral C1-2 joint PRF application in comparison with other approaches. PRF application at 45 V, 2 Hz, and 10 ms cycles for 10 minutes produces both early and late changes in the lateral C1-2 joint primary pain receptors and nerve endings. This extended electric field effects are also likely to have similar changes to the deep cervical prevertebral plexus and its branches, producing the observed increased duration of pain relief.

Conclusion

We conclude that PRF application of the lateral C1-2 facet joint is a feasible and safe technique in patients with cervicogenic headaches that are nonresponsive to other techniques such as radiofrequency denervation of lower cervical facet joints and cervical epidural injections. However, further prospective trials are required to validate this. In fact, we believe that this technique should be considered earlier in the course of the disease in view of its long-term efficacy as well as the possibility of improved efficacy if treated earlier.

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Chapter 3

Whiplash Patients with Cervicogenic Headache After Lateral Atlanto-Axial Joint Pulsed Radiofrequency Treatment

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Abstract

Background: Whiplash patients regard cervicogenic headache (CEH) as the most burdensome symptom of their condition. Sufferers experience a significant degree of disability from headache, associated neck pain and disability, and sleep disturbance. Lateral C1/2 joint pulsed radiofrequency (PRF) treatment has been shown to produce significant relief from headache in patients with CEH.

Objectives: The objective of this retrospective questionnaire study of 45 consecutive whiplash patients with CEH who had undergone antero-lateral atlantoaxial joint pulsed radiofrequency treatment (AA PRF) was to evaluate the treatment's long-term effects on pain-related disability and health-related quality of life.

Patients and Methods: Four questionnaires were sent to all 45 patients who had undergone AA PRF: 1) The short form-36 (SF-36); 2) The neck disability index (NDI); 3) The medical outcome scale-sleep scale (MOS-SS); 4) The headache impact test-6 (HIT-6). All 45 patients received AA PRF under fluoroscopic guidance. PRF treatment was conducted at 45 V with a pulsed frequency of 4 Hz and a pulsed width of 10 ms for 4 minutes.

Results: Patients who responded to the procedure reported lower pain scores at 2, 6, and 12 months of follow-up compared to nonresponders. More important, patients reported marked improvements in headache impact ($P < 0.01$), neck-disability scores ($P < 0.01$), awakening due to headache ($P < 0.01$), and sleep problems (9-item; $P < 0.05$) on the MOS-SS. Responders to the procedure also reported a significantly higher health-related quality of life in terms of bodily pain ($P < 0.05$) and health change ($P < 0.01$) on the SF-36.

Conclusions: In light of the inherent limitations of our retrospective study, AA PRF treatment can only be tentatively viewed as a promising treatment modality for whiplash patients with CEH and is subject to validation in future studies.

Background:

The term cervicogenic headache (CEH) was first coined by Sjaastad et al. in 1983. In 1990 the CHISG criteria (cervicogenic headache international study group) for CEH was issued.[1] Whiplash injuries were later implicated as likely triggers of CEH.[1] Whiplash-associated disorders (WAD) are very costly to society, and patients have rated headaches as the most burdensome WAD.[2]

The prevalence of CEH had been estimated as high as 4.1% in the general population and as high as 17.5% among patients with severe headaches. For patients with headaches after whiplash, the prevalence is as high as 53%.[3-5] Most CEH sufferers experience a significant degree of disability from headache, associated neck pain, and sleep disturbance. It is often the disability emanating

from CEH attacks that compromises quality of life for these patients. Currently, no drugs are effective for CEH. A randomized controlled study showed that manual therapy alone was no more effective than exercise alone.[6,7] Lateral C1/2 joint injections have identified the lateral C1/2 joint as a source of pain in patients with CEH.[8-9] Narouze et al.[10] found that 25% of their patients experienced 50% pain relief within 3 months. In a retrospective study with 86 patients, pulsed radiofrequency (PRF) application on the antero-lateral C1/2 joint (AA PRF) produced long-term pain relief up to 6 months, with more than 50% of patients experiencing pain relief of more than 50%.[11]

Using cervical zygapophysial joint pain as a model for chronic neck pain, Wallis and colleagues showed that all patients who obtained complete pain relief exhibited resolution of their preoperative psychological distress, whereas those who were unrelieved continued to demonstrate signs of psychological distress.[12]

Box 1. Clinical Criteria Used in Our Center for the Diagnosis of CE Attributable to Whiplash Injury

	Clinical Criteria for Cervicogenic Headache Attributable to Whiplash Injury
1	Predominantly unilateral headache without side-shift
2	Symptoms and signs of neck involvement: pain triggered by neck movement or external pressure of the posterior neck or occipital region; ipsilateral neck, shoulder, and arm pain; reduced range of motion.
3	Pain episodes of varying duration or fluctuating continuous pain
4	Moderate, non-excruciating pain, usually of a non-throbbing nature
5	Whiplash injury sustained prior to onset of headache with no obvious neurological deficit (Grade II Quebac Task Force classification)
6	No direct head injury or any loss of consciousness

Objectives

This retrospective questionnaire study of 45 WAD patients with CEH who had undergone antero-lateral C1/2 joint PRF application (AA PRF) more than 1 year ago aimed to evaluate its AA PRF's effects on pain-related disability and health-related quality of life.

Patients and Methods

Institutional review board approval was obtained prior to administering the questionnaire to all patients. This retrospective questionnaire study included 45 consecutive whiplash patients who had undergone lateral C1/2 joint PRF application for CEH in a single pain center in the Netherlands between January 2007 and February 2009. The patients were recruited from a review of the pain center's procedure records and verified with the individual patient's medical records. All 45 patients who had fulfilled clinical criteria specified in Box, had

undergone cervical facet denervation (C3 to C5) prior to the antero-lateral C1/2 PRF with minimal improvement. The lateral C1/2 joints in these 45 patients were found to be extremely tender, even after cervical facet denervation. All 45 patients were sent four questionnaires that included the Short Form-36 (SF-36)[13], neck disability index (NDI)[14], the medical outcome scale-sleep scale (MOS-SS)[15], and the headache impact test-6 (HIT-6)[16]. All four questionnaires have been established for reliability and validity in the Dutch population.[17-20] The patients were also sent a general personal data form that included a dichotomous question of whether they had experienced more than 50% pain relief after receiving the lateral C1/2 joint (AA PRF) injection. After all questionnaires were returned, post-AA PRF progress was evaluated by retrospectively retrieving pain scores (numerical rating scale of 0 to 10) of all 45 patients from individual case files. The NRS scores were retrieved at 2, 6, and 12 months. These data were all collected by an assistant not involved in the design of the study or in the analysis of the data.

The technical details of the percutaneous procedure have been described elsewhere.[11] A 22-G, 45-mm insulated radiofrequency needle with a 5-mm active tip was introduced percutaneously, under fluoroscopic control, so that it entered the lateral 1/3 of the of the antero-lateral C1/2 joint (Figure 1). Guided by fluoroscopy, it is important that the noninsulated needle tip does not contact either intra-articular osseous surface of the lateral C1/2 joint. This is to avoid causing the patient unnecessary pain during sensory stimulation. With the active tip within the intra-articular space, sensory stimulation at 50 Hz up to 1.0 V and motor stimulation at 2 Hz up to 1.0 V is almost always negative. PRF application at 45 V was then initiated with a pulse frequency of 4 Hz, pulse duration of 10 ms for 4 minutes. We do not routinely give contrast, local anesthetic, or steroids either before or after the PRF application.

For the analysis of the MOS sleep scale, 90% completion of a section was considered sufficient for analysis. The HIT-6 and NDI scores were excluded if one item was missing. For the SF-36 subscale scores, missing values were substituted with group mean values in accordance with the instructions in the SF-36 manual. All statistics were performed using SPSS (version 16.0 for Windows). Descriptive statistics were generally reported as mean values ± 1 standard deviation (SD) and were analyzed for their degree of skewness or kurtosis. A student's t-test (continuous variables) and Chi-square test (for dichotomous variables) were used to compare the differences in baseline characteristics and study measures between both groups. Pearson's correlation coefficients were used to evaluate the correlation between questionnaire scores and their relevant domains. A significance level of $P < 0.05$ was used for all tests.

Results

Thirty-six patients returned their questionnaires within 4 weeks. We attempted to contact the remaining 9 patients. Four patients returned their questionnaires after 2 reminders (88.9%). We were unable to contact 1 patient. One patient agreed to the HIT-6 over the phone but not the rest of the questionnaires. Three patients agreed to the use of retrospective data but not to the questionnaires. Forty patients completed the SF-36 and NDI questionnaires, 39 patients completed the MOS-SS questionnaires, while 41 patients completed the HIT-6 questionnaires. Of the 44 patients who consented to the study, 25 patients self-reported more than 50% pain relief at the time of the survey and were denoted as treatment responders (hereafter, responders). The remaining 19 patients reported less than 50% pain relief at the time of the survey and were denoted as treatment nonresponders (hereafter, nonresponders). The responders' post-AA PRF improvement in pain scores was consistently lower than the scores of the nonresponders at 2, 6, and 12 months (Table 1; $P < 0.05$). The baseline demographic characteristics of the responders and nonresponders did not differ significantly (Table 2). Additionally, the history of postprocedure employment, litigation, and government benefits did not differ either; the only demographic characteristic that did vary significantly was the age of the responders ($t = -1.95$, $P < 0.058$).

The mean questionnaire scores (± SD) of both the responder and the nonresponder group are shown in Table 1. The HIT-6 and the NDI scores were significantly lower in the responder group than in the nonresponder group. The domains of awakening due to headache sleep problems Index I (6-items) and sleep problems Index II (9-items) in the MOS-SS were all significantly lower in the responder group than in the nonresponder group. Responders also had higher mean scores in all domains of the SF-36 (Table 1). However, this achieved statistical significance in only 2 subscales: bodily pain ($t = -2.44$, $P < 0.05$) and perception of health change ($t = -3.60$, $P < 0.01$), with role-physical being nonsignificant ($t = -1.88$, $P = 0.68$).

The lower headache impact scores in the responder group correlated significantly with a decrease in neck disability ($r = 0.64$, $P < 0.001$) as well as with awakening due to headache ($r = 0.55$, $P < 0.01$) in the MOS-SS. The lower neck-disability score in the responder group also correlated significantly with a decrease in sleep problems and awakening due to headache (6-item: $r = 0.36$, $P < 0.05$; 9-item: $r = 0.44$, $P < 0.01$) in the MOS-SS. The perceived improvement in health correlated well with a reduction in the impact of headaches on life ($r = -0.54$, $P = 0.001$), neck disability ($r = -0.50$, $P = 0.001$), and bodily pain ($r = 0.67$, $P < 0.001$).

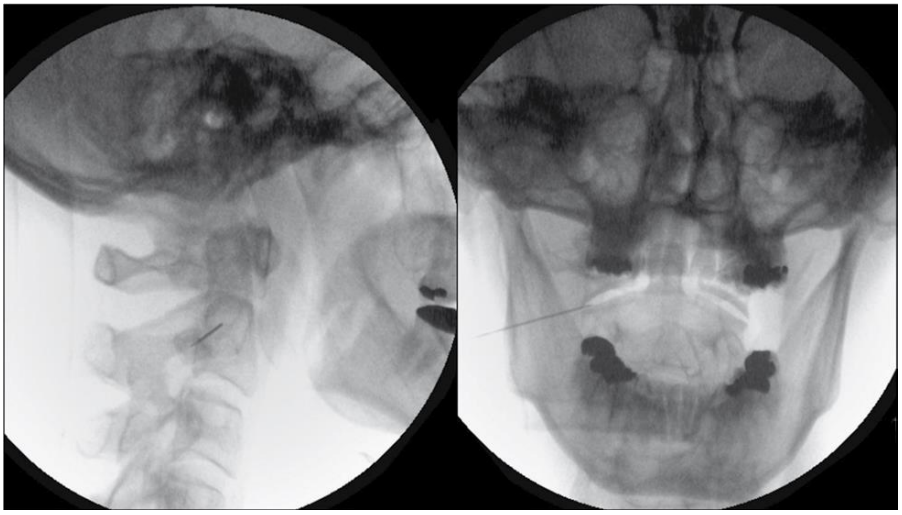

Figure 1. Lateral View With a 5º Oblique Tilt for Initial Needle Entry (Left). Postero-Anterior View (Right) of Needle Entry into Lateral C1/2 Joint. Notice the Active Tip Does Not Contact the Intra-Articular Osseous Surface.

Discussion

From our retrospective findings, patients with sustained pain relief after AA PRF experienced improvements in headaches' impact on life, reductions in neck disability, improvements with respect to sleep problems, and an improved overall perception of health within 12 months after treatment. The improvements in headaches' impact on life were also highly correlated with improvements in neck disability and sleep.

Table 1. Questionnaire and Pain (NRS) Scores

	Responder Group (n = 25)	**Non-Responder Group (n = 19)**	**t score**	**P value**
HIT-6 [a], Mean ± SD	56.7 ± 11.7	68.6 ± 7.1	4.02	< 0.001 [b]
NDI [a], Mean ± SD	18.9 ± 8.4	27.1 ± 7.4	3.27	0.002 [b]
MOS-SS [a], Mean ± SD				
Sleep disturbance	44.8 ± 24.9	55.3 ± 25.3	1.30	0.203
Snoring	42.9 ± 28.5	29.4 ± 33.3	-1.32	0.196
Headache	44.5 ± 30.2	72.9 ± 28.2	3.02	0.005 [b]
Sleep adequacy	43.2 ± 28.7	32.4 ± 27.0		0.235
Somnolence	35.8 ± 25.9	46.7 ± 20.7	-1.21	0.152
Sleep problems index I	41.2 ± 10.4	48.2 ± 9.1	1.46	0.030 [b]
Sleep problems index II	42.5 ± 13.2	51.1 ± 10.7	2.25	0.031 [b]
			2.24	
SF-36, Mean ± SD				
Physical functioning	63.9 ± 23.9	57.4 ± 18.2	-0.98	0.331
Role-physical	37.0 ± 43.2	16.2 ± 26.4	-1.88	0.068
Bodily pain	55.8 ± 23.0	41.1 ± 15.3	-2.44	0.020 [b]
General health	53.3 ± 23.3	49.7 ± 21.8	-0.50	0.623
Vitality, Mean ± SD	46.5 ± 21.8	42.4 ± 17.0	-0.68	0.500
Social functioning, Mean ± SD	61.4 ± 25.3	57.4 ± 16.0	-0.62	0.538
Role-emotional, Mean ± SD	76.8 ± 38.2	58.3 ± 41.3	-1.42	0.166
Mental health, Mean ± SD	70.3 ± 20.6	64.7 ± 18.6	-0.89	0.379
Perceived health change, Mean ± SD	65.2 ± 26.9	39.7 ± 17.8	-3.60	0.001 b
NRS a scores, Mean ± SD				
0 month	8.68 ± 0.78	8.32 ± 0.82	1.46	0.153
2 months	1.64 ± 1.53	6.00 ± 2.85	-5.98	< 0.001 [b]
6 months	1.68 ± 1.89	6.53 ± 2.41	-7.08	< 0.001 [b]
12 months	1.45 ± 1.41	7.74 ± 1.32	-14.71	< 0.001 [b]

[a] Abbreviations: HIT-6; headache impact test-6; MOS-SS, medical outcome scale-sleep scale; NDI, neck disability index; NRS, numerical rating scale

[b] Denotes comparisons that are statistically significant at P < 0.05

Table 2. Baseline Characteristics of Treatment Responders and Nonresponders to Antero-Lateral C1/2 Joint PRF[a]

	Non-responders (n = 19)	Responders (n = 25)	P value
Age, y, Mean ± SD	41 ± 13	49 ± 11	0.05
Gender, No.			0.68
Male	11	16	
Female	8	9	
Height, cm, Mean ± SD	174 ± 9	171 ± 7	0.25
Weight, kg, Mean ± SD	73.1 ± 14.5	70.0 ± 15.3	0.81
Secondary education and above, No.	3	7	0.32
Smoke, No.	7	4	0.12
Alcohol, No.	7	10	0.79
Years of pain, Mean ± SD	6.9 ± 9.4	7.1 ± 3.5	0.66
Pre-procedure numeric rating scale (NRS)-score, Mean ± SD	8.4 ± 0.8	8.6 ± 0.8	0.38
Involved in litigation prior to procedure, No.	2	4	0.59
Years post-procedure, Mean ± SD	2.0 ± 0.5	1.7 ± 0.7	0.39
Currently employed, No.	9	10	0.59
Returned to work, No.	10	11	0.82
Benefits act from work loss or injury, No.	7	7	0.52

[a] Abbreviation: PRF, pulsed radiofrequency

The divergent pain scores between the responders and nonresponders at 2, 6, and 12 months after AA PRF were reinforced by a self-reported improvement in general health by the responders. Despite consistently higher scores in all the health-related, quality-of-life domains, we were limited by a relatively small sample size to detect significant improvements in those who responded to AA PRF. We are unable to conclude that the extended duration of pain relief observed in the responder group is entirely a result of antero-lateral C1/2 joint PRF due to inherent limitations in our retrospective study. However, our findings suggest that if whiplash patients with CEH do respond to intra-articular lateral C1/2 joint PRF, they may not only improve in terms of pain scores but also may exhibit positive changes to life burdens, neck-related disability, and perceived health over the long term.

An extensive body of research is looking at the mechanisms through which PRF acts. At the time of this writing, most studies point towards an alteration in synaptic transmission in a neuromodulatory-type effect.[21,22] The effects of PRF were initially postulated to be via a combination of excitatory C-fibre response suppression as well as inhibition of synaptic transmission with the decrease in excitatory postsynaptic potential.[22-24] However, in intra-articular PRF, this is unlikely to be the case: the effects of intra-articular PRF are most likely a result of its anti-inflammatory properties. This occurs as a result of the attenuation of proinflammatory cytokines such as interleukin (IL)-1b, tumor necrosis factor a (TNF-a), and IL-6 by the generated electric fields.[25,26] In fact, IL-1b, which is

present in high amounts in OA cartilage, is considered to be one of the main catabolic factors involved in the cartilage matrix degradation.[27,28] In addition, an up-regulation of adenosine A2a receptor density has been observed in human neutrophils treated with pulsed electric fields.[29] Activation of adenosine A2a receptors seems to be associated with inhibition of the catabolic cytokines TNF-a, IL-6, and IL-8.[30,31] It seems intuitive to presume a similar mechanism of action of the A2a receptor on chondrocyte membranes, with a similar consequential effect of cytokine inhibition.[27,31]

One of the hypotheses generated from this retrospective study is thus the chrondro-protective mode of action of intra-articular PRF, which may explain the anecdotal observation of pain relief 2 to 4 weeks after PRF in a number of patients. A number of in-vitro studies have shown that chondrocyte proliferation and matrix synthesis are significantly enhanced by pulsed electrical fields.[28,32-34] Fini *et al.*[27] suggest that the delivery of pulsed electromagnetic fields combines an anabolic effect on chondrocytes, a catabolic cytokine blockage, a stimulatory effect on anabolic cytokine production, and a counteraction of the inflammatory process in osteoarthritis. Cosman *et al.*[35] assert that magnetic fields generated in PRF are negligible and any therapeutic effects are due to the electric fields. More research will therefore be required to verify in-vitro effects, if this hypothesized chondro-protective mechanism is indeed true.

The main limitation of our study is the lack of a control group. The retrospective nature of the study and the relatively small sample size also prevent strong conclusions regarding the efficacy of antero-lateral C1/2 PRF for whiplash patients with CEH.

As we attempt to prospectively evaluate our results in a formal trial, more studies will be also needed to evaluate other treatment modalities in this multifaceted clinical diagnosis. It seems prudent to adopt an algorithmic approach in the management of such patients, and at the time of this writing, antero-lateral C1/2 joint PRF should be at most be regarded as a potentially viable treatment modality subject to validation in future studies.

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Chapter 4

Pulsed Radiofrequency Treatment for Trigeminal Neuralgia

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Abstract

Background: Pulsed radiofrequency (PRF) treatment is defined as the delivery of short pulses of radiofrequency via a needle tip, which does not result in an actual thermal lesions. There are mixed views regarding the use of PRF for trigeminal neuralgia (TN). In our opinion, one of the main reasons for the contrasting views is the insufficient PRF dose employed in previous studies. In a recent study on the effects of PRF on resiniferatoxin induced neuropathic pain in an animal model, the anti-allodynic effects of PRF were significantly greater when the PRF exposure duration was increased from 2 to 6 minutes.

Objectives: The primary objective of this retrospective study is to report the results for 36 consecutive patients who underwent PRF treatment for TN, for 6 minutes at 45 V at a pulsed frequency of 4 Hz and a pulse width of 10 ms.

Patients and Methods: For the study, we obtained procedural records of 36 consecutive patients. Their current state of pain was evaluated over a telephonic survey and the post-procedural data at 2, 6, and 12 months were retrieved thereafter from the patient records. The main outcome measure was excellent pain relief (more than 80%), which was assessed at 2, 6, and 12 months.

Results: The percentages of patients who showed excellent pain relief (> 80% pain relief) at 2, 6, and 12 months were 73.5% (25/34), 61.8% (21/34), and 55.9% (19/34), respectively. The percentages of patients showing satisfactory pain relief (50–80% pain relief) at 2, 6, and 12 months were 14.7% (5/34), 17.6% (6/34), and 17.6% (6/34), respectively, and those of patients showing less than satisfactory pain relief (< 50% pain relief) at 2, 6, and 12 months were 11.8% (4/34), 20.6% (7/34), and 23.5% (8/34), respectively. No complications were reported, and none of the patients required hospitalization.

Conclusions: PRF of the trigeminal ganglion should be further evaluated as an alternative treatment method for TN.

Background

The International Headache Society classifies trigeminal neuralgia (TN) into classical and symptomatic TN, with the latter being clinically indistinguishable from the former. The only identifiable difference between the 2 conditions is that in symptomatic TN, a causative lesion (other than vascular compression) can be detected, and has been demonstrated in imaging or posterior fossa exploration (International Classification of Headache Disorders-II).[1] In clinical practice, 2 phenotypic forms of TN are usually recognized, typical and atypical TN.[2-4] The hallmark of typical TN is paroxysmal pain, which is lancinating in nature and occurs unilaterally in a trigeminal distribution.[5] Paroxysmal pain is present in atypical TN as well, but patients often report it along with diffuse and chronic pain, which

persist beyond the duration of a typical paroxysm, in the same trigeminal distribution areas. The paroxysmal pain distinguishes atypical TN from persistent idiopathic facial pain, which was previously known as atypical facial pain.[1] Carbamazepine is the drug of choice in the initial treatment of idiopathic TN. However, some patients develop adverse effects while some others do not show sustained pain relief.[5] For cases in which conservative treatment is not successful, invasive treatment can be considered. The available options include surgical microvascular decompression (MVD)[6,7], surgical sectioning of a portion of the sensory component of the trigeminal nerve, stereotactic radiation therapy or gamma knife treatment[8], percutaneous balloon microcompression[9], percutaneous glycerol rhizolysis[10], and percutaneous radiofrequency (RF) thermocoagulation of the Gasserian ganglion[11]. In addition to the operative risks inherent in surgical techniques, all neurodestructive methods present risks of sensory loss, dysesthesia, anesthesia dolorosa, corneal anesthesia, and facial muscle weakness.[12,13]

Pulsed radiofrequency (PRF) treatment is defined as the delivery of short pulses of RF via a needle tip, thereby avoiding thermal lesions. This technique had been performed for various other conditions and has been shown to be effective and safe. There are contrasting opinions regarding the use of PRF treatment for TN[14,15], but in our opinion, one of the main reasons for this discrepancy is the insufficient PRF dose used in most studies.

Objectives

In a recent study on the effects of PRF on resiniferatoxininduced neuropathic pain in an animal model, the anti-allodynic effects of PRF were significantly greater when the PRF exposure duration was increased from 2 to 6 minutes.[16] We present a retrospective study of 36 patients with TN who underwent PRF treatment of the trigeminal ganglion for 6 minutes at 45 V, pulse frequency of 4 Hz, and pulse width of 10 ms.

Patients and Methods

3.1. Subjects

Institutional research review board approval was obtained prior to the retrospective collection of patient data. All patients presenting at our hospital with refractory facial neuralgia undergo a multidisciplinary assessment, including complete neurological evaluation and magnetic resonance imaging (MRI). This retrospective study included all 36 patients who underwent lateral trigeminal ganglion PRF treatment for typical and atypical TN at a single pain centre from January 2007 to April 2009. All the therapeutic procedures were performed by 2 pain physicians at

our pain centre. A referring neurologist excluded secondary causes of the pain after studying MRI reports. All 36 patients presented with lancinating, burning, or aching unilateral severe facial pain, in one or more of the trigeminal nerve distributions; a small proportion of patients also experienced chronic background pain. Typical trigger points on the face in one or more of the trigeminal nerve distributions were observed in both patients with typical and atypical TN. Distinct triggering stimuli or activities such as touch, cold wind on the face, chewing, talking, and yawning were also commonly reported. Many of the painful episodes or paroxysms lasted from minutes to hours, but the episodes rarely lasted for days. Some patients reported that initial treatment with drugs such as carbamazepine, phenytoin, or gabapentin was effective, but their pain relief was rarely sustained.

3.2. Procedure

The percutaneous technique was performed as first described by Sweet et al.[11] in 1974. In this procedure, the patient lies comfortably in a supine position with the head slightly extended. Electrocardiogram and pulse oximetry and blood pressure readings are obtained for continuous hemodynamic monitoring. The C-arm is introduced in a postero-anterior fashion and rotated caudo-cranially to produce a submental view. The foramen ovale can be often already visualized with this view. A 5–10-degree tilt to the ipsilateral affected side may be required to improve visualization of the foramen ovale, as shown in Figure 1. The needle entry point is 2–3 cm from the corner of the mouth. An approach that worked well for us was to "bring the foramen ovale to the entry point" by manipulating the C-arm in a caudo-cranial orientation, which produced an excellent "tunnel view."

The skin over the needle entry point is anesthetized with 1% lidocaine. Using an aseptic technique, the needle is directed towards the ipsilateral pupil. We follow the practice of keeping 1 finger in the mouth of the patient to reduce the chance of needle entry into the oral cavity. If the oral cavity is breached, the needle is replaced to reduce the rate of infectious complications. Up to 0.75 mg/kg of propofol is used to sedate the patient during the initial needle penetration into the foramen ovale. Once the needle enters the foramen ovale into Meckel's cavity, the C-arm is then rotated laterally to ascertain the depth of penetration. The final position of the needle tip is just past the angle formed by the petrosal ridge of the temporal bone and the clivus. The propofol sedation is discontinued, the patient is allowed to awaken, and sensory stimulation is carried out at 50 Hz. The definitive position of the electrode was verified by inducing paresthesia with sensory stimulation between 0.1–0.3 V in the affected painful area. PRF is then applied for 6 minutes at 45 V, with a pulse width of 10 ms and a pulse frequency of 4 Hz. The cut-off needle tip temperature was set at 42 °C.

3.3. Patient Data Collection

In March 2010, an assistant attempted to contact all the 36 patients who had undergone lateral trigeminal ganglion PRF application for typical and atypical TN, in a single pain centre from January 2007 to April 2009, to enquire about their current status. After the telecommunication process was completed, retrospective patient data were retrieved from individual patient records. The perceived effect for each patient was recorded in the form of a Likert scale as a part of our routine clinic follow-up intervals at 2 months, 6 months, and 12 months. Perceived effect was recorded as a) less than 50% relief; b) 50–80% pain relief; c) more than or equal to 80% pain relief. The data entry was performed by another assistant who was not involved in the design of the study or in the analysis of the data. Descriptive statistics were generally reported as mean ± SD. Frequency counts were used to summarize categorical data. All statistical analyses were performed using the SPSS software package for Windows (version 16.0).

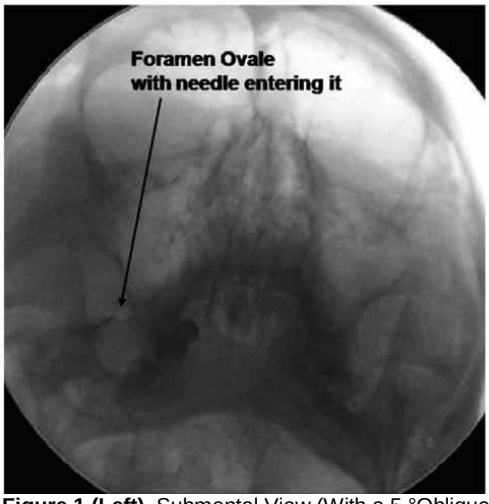
Results

The pain centre procedural records showed that 36 patients had undergone PRF treatment on the trigeminal ganglion from January 2007 to January 2009. A mean duration of 2.3 ± 0.8 years have elapsed since the last PRF procedure in this group of patients, of which 67.6% still reported satisfactory pain relief. Of these 36 patients, 1 died and 1 underwent a neurosurgical procedure soon after the PRF and was unwilling to participate in the evaluation. The remaining 34 patients consented to the use of their retrospective data for analysis. The baseline characteristics of the 34 patients are shown in Table 1. The distribution of the affected trigeminal branches is shown in Figure 2.

Table 1. Baseline Characteristics of Patients Who Underwent Trigeminal Ganglion PRF[a]

Baseline Characteristics	Patients, (n = 34)
Gender, No. (%)	
Males	**11 (32.4)**
Females	**23 (67.6)**
Age, y, Mean ± SD	73 ± 14
Duration of pain, y, Mean ± SD	7.2 ± 6.2
VAS a before TG a PRF a, Mean ± SD	8.7 ± 0.7

[a] Abbreviations: PRF, pulsed radiofrequency; TG, trigeminal ganglion; VAS, visual analogue scale



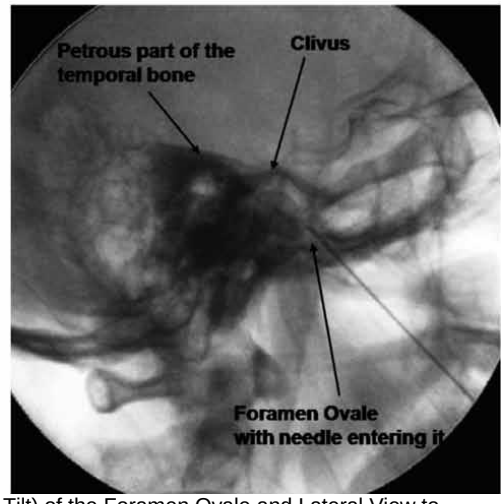


Figure 1 (Left). Submental View (With a 5 °Oblique Tilt) of the Foramen Ovale and Lateral View to Confirm the Depth of Needle Insertion
Figure 2 (Right). Distribution of Affected Trigeminal Branches

From the retrospective review of the documented clinical results of all 34 patients, the percentages of patients who showed excellent pain relief (≥ 80% pain relief) at 2, 6, and 12 months were 73.5% (25/34), 61.8% (21/34), and 55.9% (19/34), respectively. The percentages of patients with satisfactory pain relief (50–80% pain relief) at 2, 6, and 12 months were 14.7% (5/34), 17.6% (6/34), and 17.6% (6/34), respectively, and those of patients showing less than satisfactory pain relief (< 50% pain relief) at 2, 6, and 12 months were 11.8% (4/34), 20.6% (7/34), and 23.5% (8/34), respectively. No complications were reported, and none of the patients required hospitalization.

Discussion

To our knowledge, this is the largest series of TN patients treated with PRF. Among these patients, 67.6% continued to report satisfactory pain relief after 2.3 ± 0.8 years of PRF treatment. This data correlated well with our records of excellent and satisfactory rates of pain relief at 6 and 12 months. This may mean that good pain relief at 6–12 months after trigeminal ganglion PRF treatment may predict for long-term efficacy using PRF treatment. The affected trigeminal branch distributions in all 34 patients in our series were similar to those reported in the literature.[5,17]

In a prospective case series, reported by Van Zundert et al.[14], 5 high-risk patients received administered PRF treatment for the trigeminal ganglion. The first 4 patients experienced excellent pain relief over an average of 17.5 months, even though 1 of them required a repeat procedure. In patient 5, despite a reduction in

pain intensity and frequency, the patient received conventional RF rhizotomy of the trigeminal ganglion at another centre 5 months later, with only minimal relief. This patient was eventually referred for microvascular decompression after 26 months. Our findings for this small but well-conducted case series reinforce the potential efficacy of PRF treatment in TN.

In the largest review till date, Kanpolat et al.[13] reported the results for 1,600 patients who had undergone percutaneous RF trigeminal rhizotomy over a period of 25 years. The complications reported in this large study were decreased corneal reflex (5.7%), weakness and paralysis of the masseter muscle (4.1%), dysesthesia (1%), anesthesia dolorosa (0.8%), keratitis (0.6%), and temporary paralysis of the third and fourth cranial nerves (0.8%). Complications like anesthesia dolorosa, though considered rare by some, are regarded to be worse than the initial pain of TN. It was perhaps for this reason that PRF was explored as a less risky alternative. However, Erdine et al.[15] demonstrated in a double-blinded trial that PRF was remarkably less efficacious that conventional RF. Their results demonstrate significant pain reductions in all patients treated with conventional RF, while only 2 of the 20 patients in the PRF group experienced this level of pain relief. We wish to highlight some pertinent observations that may explain the lower efficacy in the PRF group in comparison with the efficacy in the conventional RF group in that study.

The authors in that trial used the well-accepted meticulous process of conventional RF of the trigeminal ganglion. RF thermocoagulation at 70 °C for 60 s was carried out, and the sensitivity of the affected area of the face and cornea were tested thereafter. If more than 1 branch of the TN was affected, second or more procedures were performed by repositioning the needle tip and waiting for paresthesia after each procedure. Such a meticulous process, however, was not described for PRF. It appears that they performed a PRF treatment procedure, wherein 2 bursts of 20 ms were applied for 120 s at an output of 45 V.[15]

Notwithstanding the different end-points of both treatments, we feel that an unfair comparison had been made with regard to 2 aspects:

1) Similar to RF, if more than 1 branch of the trigeminal nerve is affected, PRF application to other affected trigeminal distributions is equally important.

2) In our experience, PRF treatment with a pulsed width of 20 ms and frequency of 2Hz for 2 minutes is insufficient for TN.

In the case series by Van Zundert et al.[14], 1 patient who required a second procedure had more than 1 trigeminal branch. Even in our retrospective study, 5 out of 34 patients (14.7%) required more than one session of PRF treatment. The reason for this could be due to the neuromodulatory mode of action of PRF, which does not produce immediate paresthesia as in RF thermocoagulation. With regards to the second point, we applied PRF at 45 V, with a pulsed width of 10 ms, and a

pulsed frequency of 4 Hz for 6 minutes. This higher PRF dose has recently been validated in an animal neuropathic pain-model study whereby PRF was applied to the sciatic nerve 1 week after induced injury for 2, 4, and 6 minutes.[16] The group where PRF was applied for 6 minutes showed increased withdrawal latency-increased anti-allodynic effects, than the groups with 2 or 4 minutes of PRF application.

A systematic review of ablative neurosurgical techniques for the treatment of TN evaluated 166 studies reporting RF thermocoagulation, glycerol rhizolysis, balloon compression of the trigeminal ganglion, and stereotactic radiosurgery and concluded that RF thermocoagulation offers the highest rates of complete pain relief.[2] In our opinion, RF trigeminal rhizotomy is still an invaluable technique that has provided pain relief for many patients with TN. In our opinion, PRF needs to be performed to a similar degree to be compared in the same light. It may be prudent to even consider performing PRF prior to RF for a sole purpose of avoiding disturbing sensory paresthesia and masseter paralysis.

The limitations of this study are inherent to retrospective studies of such nature, in which data have been collected in a clinical context and cannot, for example, allow quantification of the changes in pain medications over 1 year of follow-up. PRF treatment of the trigeminal ganglion may be a possible alternative to minimally invasive treatment in the management of TN. The possibilities of reduced heat-related complications and comparable efficacies to conventional modalities need to be evaluated in greater detail in further studies.

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Chapter 5

The Long-Term Efficacy and Safety of Percutaneous Cervical Nucleoplasty in Patients with a Contained Herniated Disc

Halim W, Wullems JA, Lim T, Aukes HA, van der Weegen W, Vissers KC, Gültuna I, Chua NH.

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Abstract

Background: Percutaneous cervical nucleoplasty (PCN) is a safe and effective treatment in symptomatic patients with contained cervical herniated disks. It provides simple and efficient disk decompression, using a controlled and highly localized ablation, but evidence regarding long-term efficacy is limited. We conducted a retrospective study to investigate the long-term efficacy and safety of PCN, and the influence of ideal selection settings.

Methods: A total of 27 patients treated with PCN fulfilling ideal selection criteria (Group A) were studied and compared to 42 patients not meeting these criteria (Group B). Outcomes were assessed using the Visual Analogue Scale (VAS) and a four-level Likert item for perceived pain and satisfaction, the Neck Disability Index (NDI), and the Short Form 36 (SF-36). Additional relevant outcomes were retrieved from medical records.

Results: The postoperative mean VAS pain for Group A was 29.9 (SD ± 32.6) at a meanfollow-up of 24 months (range: 2–45). Only 10% of these patients reported mild transient adverse events. There was a trend, but no difference between both groups in pain scores; however, treatment satisfaction was higher for Group A (74.1 ± 27.2–55.5 ± 31.4, P = 0.02). Group A also reported better physical functioning based on the Physical Component Summary (43.6 ± 10.6–37.3 ± 12.0, P = 0.03) and showed a larger proportion of patients no longer using any medication postoperatively (63–26%, P = 0.01).

Conclusion: These results show long-term effectiveness and safety of PCN in patients with a one-level contained cervical herniated disk, and the reliance of selecting patients meeting ideal criteria for successful PCN.

Introduction

Pain stemming from intervertebral disk pathology is difficult to manage and is costly to healthcare organizations around the world.[1,2] Pain from intervertebral disks may be caused by mechanical compression from extruded disk material, accompanying inflammatory response, and released chemical mediators.[3]

The move toward minimally invasive spine surgery is partially driven by various factors including the desire to reduce surgery-related trauma, patients' awareness of alternatives to open surgical procedures, and the development of new technologies.[1,2,4–6] Disk decompression relieves symptoms in patients with contained herniated disks at both the cervical and lumbar spine.[7] Chemical, mechanical, and thermal methods have been utilized, and percutaneous cervical nucleoplasty is one such method.[7] Its basic principle is that a small reduction in volume in a hydraulic space, like an intact disk, results in a disproportionately large fall in pressure. Ablation of approximately 1 mL of disk tissue volume corresponds to a diskal pressure reduction of about 10–20%,[4–6] resulting in a reduction in pain.[6] It is a minimally invasive procedure aimed at relieving pressure on sensory structures while minimizing trauma to normal tissues and enhancing patient recovery.[1,5,6]

Studies have demonstrated percutaneous cervical nucleoplasty (PCN) to be both safe and effective.[1,3–7]

Strict patient selection is believed to be of significant importance for successful treatment.[3,6] PCN uses Coblation Technology[6] whereby a portion of the nucleus tissue is ablated using a 1-mm-diameter bipolar instrument that creates radiofrequency energy.[6] This results in ablation of a portion of nucleus tissue with a lowtemperature (typically 40–70°C) plasma field of ionized particles.[2,6] These particles have sufficient energy to break down organic molecular bonds within the tissue, dissolving the soft tissue material of the disk nucleus.[2,6] The procedure provides a simple and efficient disk decompression method, using a controlled and highly localized ablation, with minimal damage to surrounding healthy tissue.[2,4,6,7] There is little information on the long-term outcomes after PCN.[2,7] The primary objective of this retrospective study was to evaluate the long-term efficacy of PCN based on degree of pain relief, patient satisfaction, functional improvement, usage of pain medications, and incidence of adverse events, in symptomatic patients with one-level contained cervical herniated disk complaining of radicular pain. The secondary objective of this study was to evaluate the influence of nonideal patient factors in postprocedure outcomes when compared to ideal selection settings.

Patients and methods

Due to the retrospective study design, this study was exempted from review by an institutional review board under Dutch national law.

Patient Population

One hundred twenty-one consecutive PCN procedural records from 2 general district hospitals in the Netherlands, performed between May 2007 and July 2011 on 115 patients, were reviewed, and the workflow is shown in Figure 1. Thirty-eight patients with a singlelevel contained cervical herniated disk diagnosed on preoperative Magnetic Resonance Imaging (MRI) and confirmed by a diagnostic selective nerve root block were identified. These patients failed conservative therapy and complained mainly of radicular pain with or without neck pain (Group A). We considered these as the most important selection criteria for successful PCN. Sixty-five patients who were treated with PCN, but did not fulfill all these criteria, were identified (Group B). These patients, either or not with previous neck surgery, formed a mixed group of indications based on preoperative MRI findings of either multi- level cervical discopathy, disk prolapse with an extruded or sequestrated disk fragment, bulging disk only with no clear evidence of herniation, spinal canal stenosis, uncovertebral arthrosis, hypertrophy of the posterior longitudinal ligament, or cervical osteophytes. All patients were sent questionnaires to assess perceived pain and satisfaction using a Visual Analogue Scale (VAS)-100 mm and a four-level Likert item. Functional outcomes and quality of life scores were measured using the Neck Disability Index (NDI)[8] and the Short Form 36 (SF-36).[9] The incidence of complications and side effects, recurrence of symptoms, and pre- and postoperative pain medication use were retrieved from medical records. Reminders by mail (twice) and by phone (once) were used to increase the response rate.

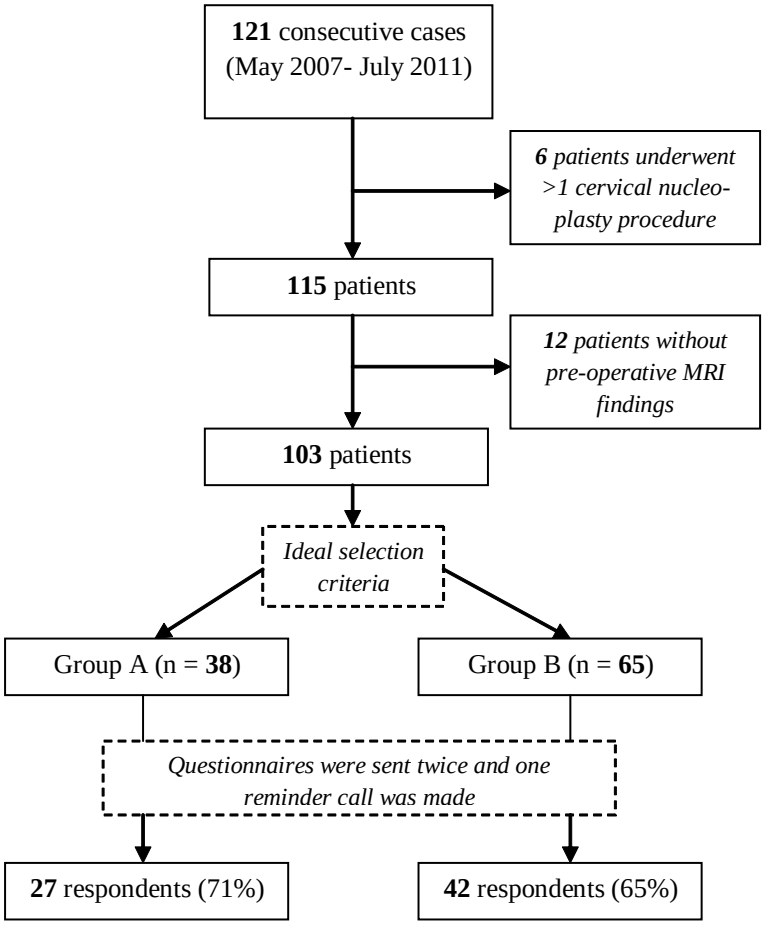

Figure 1. Flowchart of the group allocation of the study population.

Percutaneous Cervical Nucleoplasty Procedure

The protocol of the percutaneous cervical nucleoplasty procedure had been described previously.[3] Four pain physicians from the 2 different centers performed the procedures. Intravenous prophylactic antibiotics of cefazolin 1 g or augmentin 2.2 g were administered before the start of the procedure. Under aseptic conditions, a 19-gauge Trocar 3-inch spine needle (Arthro-Care Co., Sunnyvale, CA, USA) was inserted into the annulus fibrosis of the herniated disk from a 20–30° oblique approach (Figure 2). The lateral view was then used to confirm its final depth. The Perc DC SpineWand (ArthroCare Co.) was then used to create 2 small 360° lesions at different depths after coagulation check. Patients were discharged on the same day at one center, after one night stay at the other center, and a follow-up visits were scheduled 2 months after the procedure. Soft cervical bracing was applied for 3 days.

Statistical Analyses

Neck Disability Index scores were excluded if one item was missing. For the SF-36, missing values were substituted by mean group values. Data are presented as mean ± standard deviation (SD). For the comparison of baseline characteristics and study measures between group A and B, an independent samples t-test, a chisquare test, or a Fisher exact probability test was used, depending on variable type. For normal distributed data, Spearman's rank correlation coefficients were calculated to investigate correlations between the means of both the VAS pain and VAS satisfaction, and categories of reported pain change for both groups. These analyses were also performed for the categories of patient reported satisfaction in both groups. A Pearson's correlation coefficient was calculated to evaluate the correlation between the NDI and Physical Component Summary (PCS). The level of statistical significance was set at $P < 0.05$ for all tests. Statistical analyses were performed using SPSS version 19.0 (SPSS Statistics, IBM corporation, Somers, NY, USA).

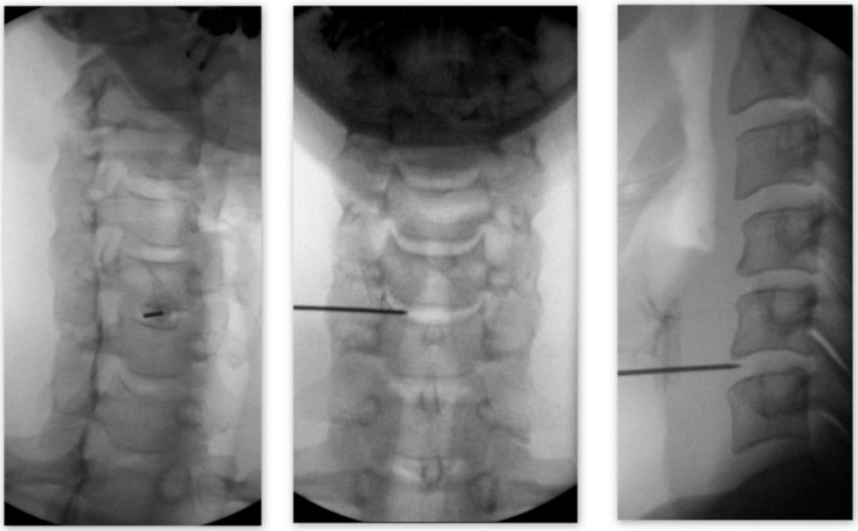

Figure 2. C-arm fluoroscopic images in oblique, anteroposterior and lateral planes of the needle onto the intervertebral disc level C4-C5. Images belong to Frank Blommers, Diagnostic radiographer, Albert Schweitzer Hospital, Sliedrecht, the Netherlands and are used after reprint request.

Results

Group A

The questionnaire response rate for Group A was 71% (16 men and 11 women patients). Mean age was 53 years (SD ± 8.0) (Table 1). Mean follow-up was 24 months (range: 2–45). Group A reported a mean VAS pain score of 29.9 (SD ± 32.6) with complete or partial pain relief in 78% of the patients (Table 2). The mean satisfaction score was 74.1 (SD ± 27.2) with 63% being satisfied or very satisfied. The VAS for pain correlated significantly with both categories of patient reported pain change ($r_s = -0.904$, $P < 0.001$) and satisfaction ($r_s = -0.891$, $P < 0.001$)

(Figure 3), and the VAS for satisfaction, respectively r_s = +0.862, P < 0.001 and r_s = +0.932, P < 0.001 (Figure 4). The NDI (n = 20) resulted in a mean neck disability percentage of 16.9 (SD ± 16.2). The SF-36 (n = 27) showed a mean PCS of 43.6 (SD ± 10.6) and Mental Component Summary (MCS) of 49.4 (SD ± 10.0). Complete details on pain medication use before and after treatment were available from 19 patients. All 19 used pain medication preoperatively. Postoperatively, almost 2/3 of all patients no longer used pain medication (63%), while usage was diminished in 16%, equal in 16%, and increased in 5%. Details on complications were retrieved from 20 patients. Two patients reported transient possible complications. One reported disturbed vision and a mild headache, which both resolved within a few days. One patient had mild tingling in the right arm and leg, which resolved later. The majority (90%) reported no complications. Four patients needed further treatment for persistent pain. One underwent cervical discectomy, another was treated with pulsed radiofrequency (PRF) first and discectomy later, the third received an epidural steroid injection, and the fourth patient received a nerve root block. Of these patients, the first 2 reported still no improvement, while the latter 2 improved.

Group A vs. B

Within Group B, 42 patients (65%) returned their questionnaires. This group consisted of 22 men and 20 women with a mean age of 50 (SD ± 7.1) years (Table 1). At a mean follow-up of 24 months (range: 3–45), the mean VAS pain score for Group B was 42.4 (SD ± 31.2) with complete or partial pain relief in 60% of the patients (Table 2). Both scores did not differ significantly from Group A. The mean VAS satisfaction was 55.5 (SD ± 31.4) with 53% being satisfied or very satisfied, resulting in a significant higher VAS satisfaction score in Group A (t = +2.45, P = 0.02). Although Group A showed a larger patient proportion being satisfied or very satisfied, this difference was not significant. Within Group B, as well the VAS pain correlated significantly with both categories of patients reporting pain change (r_s = -0.889, P < 0.001) and satisfaction (r_s = -0.870, P < 0.001) (Figure 5), as the VAS satisfaction, respectively, r_s = +0.872, P < 0.001 for both categories (Figure 6). The NDI (n = 36) resulted in a mean neck disability percentage of 27.5 (SD ± 22.5). The SF-36 (n = 42) showed a mean PCS of 37.3 (SD ± 12.0) and MCS of 49.2 (SD ± 10.7). Although a negative correlation was found between the NDI and PCS in both groups and overall (r = -0.71, P < 0.0001), only the PCS was significant higher in group A (t = +2.20, P = 0.03). Complete details on pain medication use in Group B were known from 30 patients. Three patients did not use any pain medication pre- and postoperatively, while 27 patients (90%) used pain medication preoperatively. Over 1/4 of these 27 patients did not use any pain medication postoperatively (26%), while usage diminished in 30% was equal in 33% and increased in 11%. The percentages of decrease in pain medication use did not differ between group A (79%) and B (56%).

Table 1. Baseline Characteristics

Characteristics	Group A (n = 27)	Group B (n = 42)	P value
Gender			
Male	16	22	0.58
Female	11	20	
Mean age (years)	53 (SD ± 8.0)	50 (SD ± 7.1)	0.13
Number of herniated discs per level			
C3/4	1	1	
C4/5	1	8	
C5/6	9	25	
C6/7	16	16	
Number of patients with uni-/multilevel herniation			
Unilevel	27	34	
Multilevel	0	8	
Mean duration of pain (months)	16 (SD ± 21)	37 (SD ± 35)	0.01
Mean follow-up duration (months)	24 (Range: 2–45)	24 (Range: 3–45)	0.91
Cases per follow-up term			
0–12 months (short/mid)	5	8	1.00
> 12 months (long)	22	34	

SD, standard deviation.
The Bold represents significant P-values.

Table 2. Patient Reported Outcomes

Patient Reported Outcomes		Group A	Group B	P value
Reported pain	Complete pain relief	11 (41%)	9 (22%)	0.12
	Partial pain relief	10 (37%)	16 (38%)	
	No improvement	4 (15%)	10 (24%)	
	Worse pain	2 (7%)	6 (14%)	
	Not reported	N/a	1 (2%)	
Mean VAS pain (± SD)		29.9 (± 32.6)	42.4 (± 31.2)	0.16
Reported satisfaction	Very satisfied	10 (37%)	10 (24%)	0.39
	Satisfied	7 (26%)	12 (29%)	
	Somewhat satisfied	6 (22%)	14 (33%)	
	Dissatisfied	3 (11%)	6 (14%)	
	Not reported	1 (4%)	N/a	
Mean VAS satisfaction (± SD)		74.1 (± 27.2)	55.5 (± 31.4)	**0.02**
Mean NDI (± SD)		16.9 (± 16.2)	27.5 (± 22.5)	0.08
SF-36	Mean PCS (± SD)	43.6 (± 10.6)	37.3 (± 12.0)	**0.03**
	Mean MCS (± SD)	49.4 (± 10.0)	49.2 (± 10.7)	0.94
Medicatio before	Yes	19 (100%)	27 (90%)	0.27
	No	0 (0%)	3 (10%)	
Medication after	No medication	12 (63%)	7 (26%)	**0.01***
	Less medication	3 (16%)	8 (30%)	0.10†
	Stable medication	3 (16%)	9 (33%)	
	Increased medication	1 (5%)	3 (11%)	
Complications	Yes	2 (10%)	1 (4%)	0.56
	No	18 (90%)	27 (96%)	
Further treatment needed	Yes	4 (15%)	2 (5%)	0.20
	No	23 (85%)	40 (95%)	

Abbreviations table 2: VAS, visual analogue scale; SD, standard deviation; NDI, neck disability index; SF-36, short form-36; PCS, physical component summary; MCS, mental component summary.

*No medication group A vs. B.
†No + Less medication group A vs. B.
The Bold represents significant P-values.

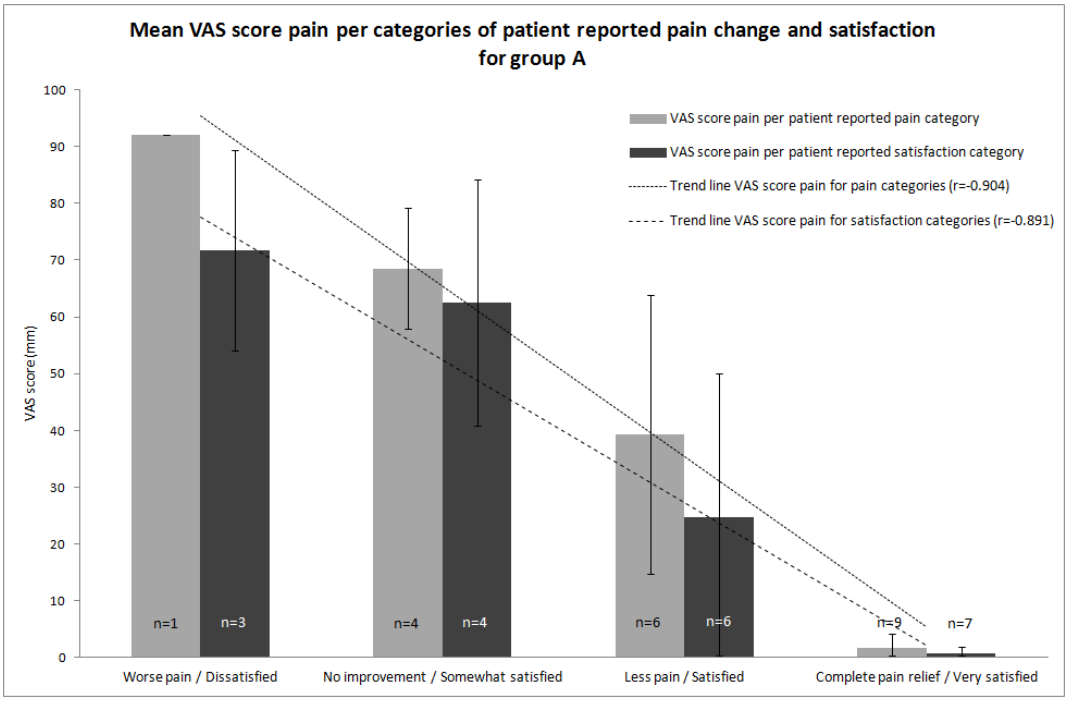

Figure 3. Categories of patient reported pain change and satisfaction representing the mean VAS score pain including added trend lines for group A.

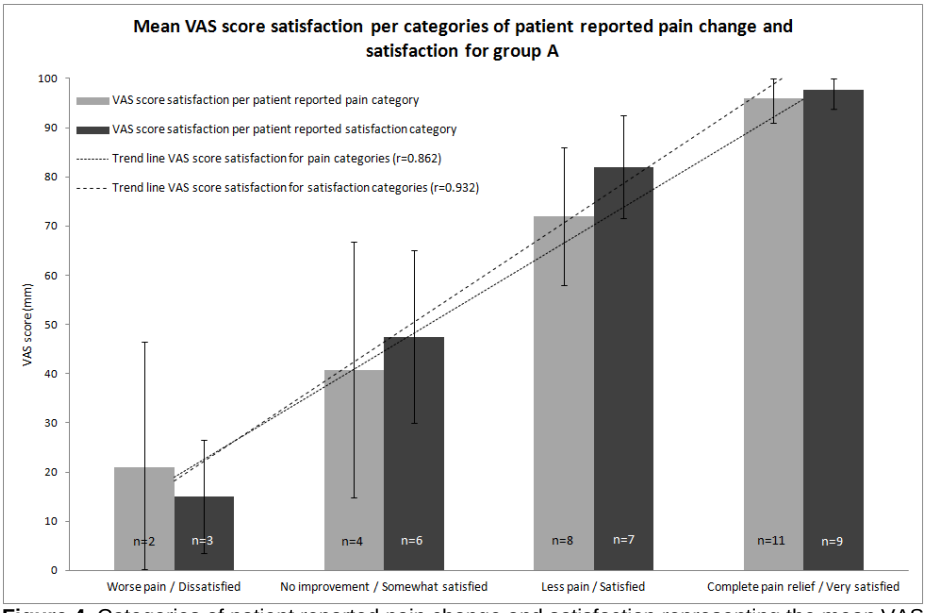

Figure 4. Categories of patient reported pain change and satisfaction representing the mean VAS score satisfaction including added trend lines for group A.

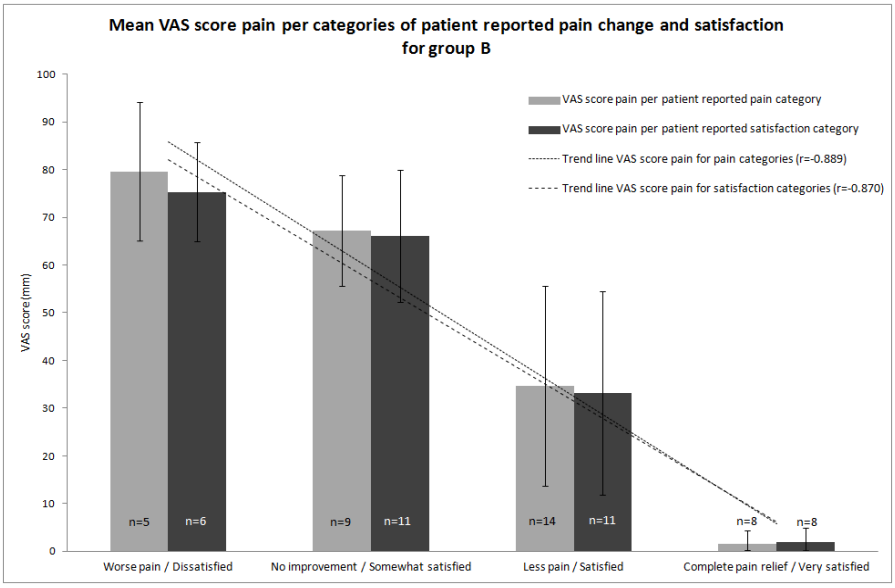

Figure 5. Categories of patient reported pain change and satisfaction representing the mean VAS score pain including added trend lines for group B.

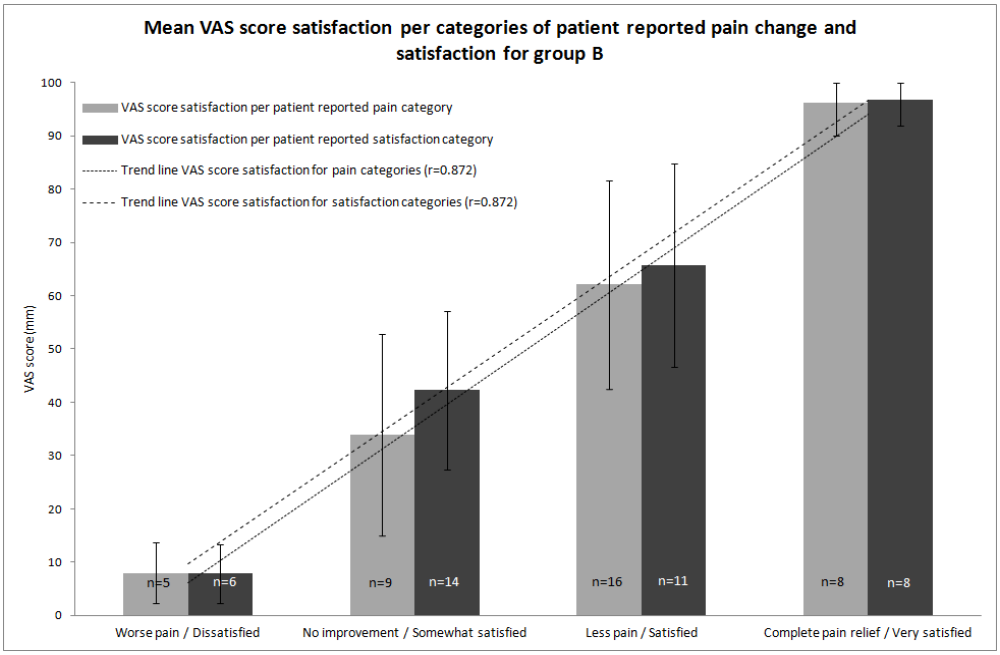

Figure 6. Categories of patient reported pain change and satisfaction representing the mean VAS score satisfaction including added trend lines for group B.

Of these proportions, 63% of Group A compared to 26% of Group B no longer used medication, resulting in a significant difference (φ = -0.37, P = 0.01). Details on complications were retrieved from 28 patients. One patient reported neck stiffness and restricted motion after treatment, but this resolved after a short period. The majority (96%) reported no complications. Percentages of reported complications differed somewhat between Groups A and B, but not significantly. Within Group B, 2 patients needed further treatment because of persistent pain. One received a cervical epidural steroid injection first and had a neuromodulator implanted later. One got a neuromodulator implanted. The first patient improved, while the latter reported still no improvement currently. There was no difference between Groups A and B in the proportion of patients requiring further treatment.

Discussion

From our results, it is clear that complete or partial longterm pain relief can be safely achieved using PCN in patients with a one-level contained cervical herniated disk. In the majority of these patients, PCN leads to long-term reduction in pain, good clinical outcomes, reduced pain medication use, and high patient satisfaction. Our results also indicate that ideal selection criteria lead to better pain relief, higher satisfaction rates, a larger reduction in the use of pain medication, and better clinical outcomes.

Our long-term high rates of pain improvement and patient satisfaction in Group A are similar to short-term results of other studies. Both Li et al.[4] and Sim et al.[3] showed a high rate of excellent and good patient satisfaction after PCN, respectively, 83.7% and 77.3%. Bonaldi et al.[10] reported successful PCN in 85% of

their treated patients. These studies reported mean postprocedure VAS pain scores ranging from 2.4 to 3.7 on a 10-cm scale, but only for short and mid-term follow-up.[3,4] A recent systematic review on effectiveness of nucleoplasty represented mean pooled VAS pain scores for short and mid-term follow-up of ± 4.0.[6] These figures agree with our result (converted to a 10-cm scale) of the mean VAS pain score for group A of 2.99. Within this group, pain medication use was diminished in 79% of the cases, and almost two-thirds of all patients did not use any pain medication at all after treatment (63%). The low complication rate found in our study is comparable to findings of several other studies.[3–5,7,11] Gertszen et al.[1] concluded that nucleoplasty appears to improve overall quality of life. They reported improvement in patients' strength and function after nucleoplasty, even after recurrence of pain. Although there is a lack of preprocedure quality of life and function scores, postprocedure scores of the SF-36 and NDI showed a normal quality of life and low neck disability percentage in group A.[12] According to literature, PCN is an effective and safe procedure. Our study confirms these main findings with long-term follow-up.

Ideal selection of patients is thought to be an element for successful nucleoplasty.[3,6] Patients with single-level incomplete annular tears and minimally degenerated disks can be expected to benefit most.[6] Patients were divided into 2 groups based on completeness of selection criteria. Patients in Group B had a wider range of indications and were believed to have more complex disk pathologies, in which a significant longer duration of pain might play a role. Comparing the long-term results after PCN of Group A with B, significant differences were found for some variables. Group B had a lower satisfaction score (55.5 ± 31.4), higher percentage (74%) of patients still using any medication postoperatively, and worse physical functioning (PCS = 37.3 ± 12.0). As there is a lack of studies focusing on selection criteria, it is difficult to compare these results; however, they confirm the recommendations in other studies.[3,6] Although physical scores were negatively correlated, indicating that a higher neck disability (NDI) is accompanied by a lower general physical function (PCS), the NDI only showed a negative trend toward group B. As the SF-36 is not a neck-specific questionnaire unlike the NDI, the results suggest that other not-specified physical issues restrict the quality of life of patients in Group B. According to the SF-36 scoring interpretation, the PCS score in Group B was far below the norm.[12] Percentages of stable or increased pain medication use were higher in Group B accompanied with a lower percentage of decrease or without any medication at all. Combined with the low PCS score, it might be a plausible explanation for the lower postoperative satisfaction in group B. This is confirmed by Galloway, et al.,[13] stating that quality of life depends on pain relief, which is linked to patient satisfaction. Although lacking evidence, the amount of pain medication is assumed to lower the actual pain scores in Group B, resulting in a clear trend of better pain scores in group A, but not significantly. PCN appeared to be a safe procedure, even regardless ideal selection. However, our results justify the recommendation of ideal selection settings for successful treatment.

Several techniques are used in the treatment for cervical disk herniation.[5] In the past, conventional cervical discectomy was considered the standard treatment.[11,14] The current evolution in spinal surgery has been toward less-invasive percutaneous techniques.[1,5,14] Nucleoplasty and PRF are important options, with

nucleoplasty most often applied.[15] Gebremariam et al.[16] concluded that no equivocal evidence for the superiority of one particular treatment exists. In general, cervical discectomy has been developed as an effective treatment for soft cervical disk herniation. It has, however, many possible drawbacks such as damage to adjacent tissue, chronic loading to adjacent disks resulting in damage and transformation, and a long recovery period.[3,5] PRF is considered as a useful alternative to nucleoplasty. It is safely used in a variety of conditions. Nonetheless, its efficacy needs to be investigated.[17–19] As research already showed high efficacy and safety of PCN with short and mid-term follow-up, this technique is preferred until remaining questions regarding PRF are answered.[17]

Strong points of our study are very strict group allocation criteria, a large number of procedures, and a long follow-up. Our findings confirm that careful indication-based patient selection is necessary to achieve better outcomes.[3,6] Due to the retrospective study design, the lack of a control group, and the lost to follow-up, our findings need to be interpreted cautiously.

We demonstrated the long-term effectiveness and safety of PCN for patients with a one-level contained cervical herniated disk in whom conservative treatment has failed. Furthermore, the importance of ideal selection settings was shown. Our findings should be confirmed in a prospective randomized clinical trial.

Acknowledgements

The authors would like to thank Tanja Hamm-Faber (Nurse practitioner, Albert Schweitzer Hospital, Sliedrecht, the Netherlands) for her contribution to the data acquisition.

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Chapter 6

Current Evidence of Percutaneous Nucleoplasty for the Cervical Herniated Disk: A Systematic Review

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Abstract

Background: Although percutaneous cervical nucleoplasty (PCN) has been shown to be both safe and effective, its application is still debated. PCN applied in disk herniation has not been systematically reviewed before, resulting in a limited insight into its effectiveness and safety, and the quality of available evidence. Therefore, we systematically reviewed the evidence on the efficacy and safety of PCN in patients with a (contained) herniated disk.

Methods: MEDLINE, EMBASE, and the Cochrane Library (Central Register of Controlled Trials) were searched for randomized controlled trials (RCTs) and nonrandomized studies using the following keywords: “Nucleoplasty,” “Cervical,” “Hernia,” “Herniation,” “Prolapse,” “Protrusion,” “Intervertebral disk,” and “Percutaneous disk decompression.” First, all articles were appraised for methodological quality, and then, RCTs were graded for the level of evidence according a best-evidence synthesis, because a meta-analysis was not possible. Finally, the RCTs’ applicability and clinical relevance also was assessed.

Results: Of 75 identified abstracts, 10 full-text articles were included (3 RCTs and 7 nonrandomized studies). These studies represented a total of 1021 patients: 823 patients (≥ 892 disks) were treated by PCN. All studies showed low methodological quality, except for two. The level of evidence of the RCTs was graded as moderate, with low to moderate applicability and clinical relevance.

Conclusion: All included studies showed PCN to be an effective and safe procedure in the treatment of (contained) herniated disks at short-, mid-, and long-term follow-up. However, the level of evidence is moderate and shows only low to moderate applicability and clinical relevance.

Introduction

Rationale

Disk pathology is an important cause of suffering and disability in the adult population, forming a difficult and costly health care issue.[1,2] Approximately, 1 person in 1000 suffers from cervical radicular pain.[3,4] Treatment options range from conservative to surgical.[5] After the exclusion of red flags (ie, cervical myelopathy, cervical fracture or instability, and cervical cancer) conventional treatment of cervical disk herniation starts with conservative care (CC) (rest, physiotherapy, and oral medications). Once conservative treatment has failed, different percutaneous, minimally invasive (radiological) procedures can relieve pain, avoiding surgery.[1] These procedures aim at relieving pressure or chemical irritation on sensory structures while minimizing trauma to normal tissues, thereby enhancing patient recovery.[6–8]

Percutaneous cervical nucleoplasty (PCN) is the most often applied technique for cervical disk decompression using Coblation technology.[1,8] The Coblation technology provides simple, efficient disk decompression, because of controlled and highly localized ablation, resulting in minimal damage to surrounding healthy tissue.[2,8–11] Several published studies have demonstrated PCN to be both safe and effective, but its application is still debated.[1,6–10,12,13] PCN applied in disk herniation

has not been systematically reviewed before, resulting in a limited insight into its effectiveness and safety, and the quality of available evidence.[5]

Objectives

The aim of this study is to systematically review the evidence on the efficacy and safety of PCN in patients with a (contained) herniated disk.

Methods

Due to the study design, this study was granted exemption by the local institutional review board.

Protocol and Registration

A review protocol was written and registered in the PROSPERO database (registration number: CRD42012002464), see: http://www.crd.york.ac.uk/PROSPERO.

Eligibility Criteria

First, randomized controlled trials (RCTs) were searched; however, as only 3 studies focusing on PCN were eligible the search was extended.[14] Hereafter, both RCTs and nonrandomized studies were identified. Only studies reporting their methods in detail, the number of patients treated, and the efficacy, complications, and follow-up (FU) term, with full text available, published from 2000 onwards, involving noncadaveric humans of age 18+ and regardless gender or race, were included.

Information Sources

MEDLINE, EMBASE, and the Cochrane Library (Central Register of Controlled Trials), respectively, were searched finally on 07 March 2013. Systematic reviews were checked for any missed studies, and reference lists of included studies were hand searched.

Search

The following keywords were included in the literature search: “Nucleoplasty,” “Cervical,” “Hernia,” “Herniation,” “Prolapse,” “Protrusion,” “Intervertebral disk,” and “Percutaneous disk decompression”. The complete search is available on request.

Study Selection

Identified abstracts were first checked for duplicate studies by 1 reviewer (JW), before 2 independent reviewers (JW, WH) screened all abstracts for eligibility. In case of disagreement, a third reviewer was consulted (WvdW). Next, the full text of the included abstracts were retrieved and assessed for eligibility by 2 independent reviewers (JW, WH). Again, a third reviewer was consulted in case of disagreement (WvdW). Finally, studies appraised as positive were included.

Data Collection Process

Data extraction was independently carried out by 2 reviewers (JW, WH). Whenever they disagreed, a third independent reviewer was consulted (WvdW).

Data Items

Before data retrieval, a study data template was designed containing the following variables: study design, number of patients, number of treated disks with PCN, alternative treatment, main effectiveness parameter(s), FU term (short term: ≤ 3 months, midterm: > 3 to ≤ 6 months, long term: > 6 months), number of reported lost to FU, number of reported complications, and final study result.

Risk of Bias in Individual Studies

To assess methodological quality, the risk of bias in individual studies was appraised. As both RCTs and nonrandomized studies were included, separate analyses were performed. RCTs were appraised using RevMan 5 (Review Manager (RevMan) [Computer program] Version 5.2. Copenhagen, The Nordic Cochrane Centre, The Cochrane Collaboration, 2012), including judgment on random sequence generation, allocation concealment, blinding of participants and personnel, blinding of outcome assessment, incomplete outcome data, selective reporting and other bias. Each item scored either low or high risk for bias. When an item was not reported in the article, it was assumed to have a high risk for bias. Based on the method described by Furlan et al.,[14] studies were considered high quality if at least 4 items scored low risk for bias. In case at least 4 items scored high risk for bias, low quality was indicated.[14] Nonrandomized studies were appraised using the Newcastle-Ottawa Scale (NOS) http://ims.cochrane.org/revman/about-revman-5. It scores 3 broad perspectives: the selection of the study groups (4 points maximum), the comparability of the groups (2 points maximum), and the ascertainment of the outcome of interest (maximum 3). As study quality resulting NOS-scoring has not been clearly defined, high quality was indicated with a NOSscore of ≥ 7 points and scoring on all 3 categories at least. Otherwise, the study quality was low.

Summary Measures

Due to the clinical heterogeneity between the included studies, it was not possible to pool the results. Therefore, a best-evidence synthesis was used to summarize the results.[5,15]

Synthesis of Results

For the best-evidence analysis, included studies were split up: RCTs were included in the primary analysis, while nonrandomized studies were analyzed separately and discussed later with the results from the primary analysis. The level of evidence of the included RCTs was appraised using a grading system as described by Gebremariam et al.[5]

Risk of Bias across Studies

To appraise the level of evidence of the included RCTs, a grading system proposed by Gebremariam et al.[5] was used. This system ranks and divides evidence into the following levels:

- Strong evidence for effectiveness: consistent (ie, at least 75% of the RCTs report the same findings) positive (significant) findings within multiple high-quality RCTs.
- Moderate evidence for effectiveness: consistent positive (significant) findings within multiple low-quality RCTs and/or 1 high-quality RCT.
- Limited evidence for effectiveness: positive (significant) findings within 1 low-quality RCT.
- Conflicting evidence for effectiveness: provided by conflicting (significant) findings in the RCTs (< 75% of the studies reported consistent findings).
- No evidence found for effectiveness of the intervention: RCT(s) available, but no (significant) differences between intervention and control groups were reported.
- No systematic review or RCT found.

Additional Analyses

As an additional analysis, the applicability and clinical relevance of the results of the included RCTs were assessed by 1 reviewer (JW) and validated by another (WH).[14] In case of disagreement, a third independent reviewer was consulted (WvdW). To determine whether study results were applicable and clinically relevant, 40 items were assessed per study, as described in the original article of Malmivaara et al.[16]

Results

Study Selection

Seventy-four abstracts were identified through database searching, and 1 additional abstract was identified by hand search. From these seventy-five abstracts, fifty-nine were unique studies of which forty-nine were excluded for not meeting our criteria. A PRISMA flow diagram for study selection is shown in figure 1.

Study Characteristics

Fifty-nine abstracts were screened of which ten full-tekst articles were included (3 RCTs, 7 nonrandomized studies). These ten studies represent a total of 1021 patients: 823 patients (≥ 892 disks) were treated by PCN (both reports of Cesaroni et al.[17,18] did not report the exact number and levels of treated disks, but only patients n = 62 and n = 349). When distracting the number of patients reported by Cesaroni et al.[17,18] (62 + 349 = 411), 481 (≥ 892 to 411) detailed PCN treated disks remain. Of these, 353 were single level, 49 were at 2 adjacent levels, and 10 were at 3 adjacent levels. The C3–C4 level was treated in 33 cases, the C4–C5 level in 93 cases, the C5–C6 level in 219 cases and the C6–C7 level in 136 cases. Four comparative studies were included; 3 RCTs and 1 retrospective study.[7,10,17,19] All

RCTs[10,18,20] compared PCN with CC (medical and/or physical therapy) (n = 103), while the retrospective study 7 compared with percutaneous cervical diskectomy (PCD) (n = 95). Total FU term ranged between 60 days and 60 months. Treatment efficacy was measured using multiple outcome scores, that is, Visual Analog Scale (VAS) score for pain, Neck Disability Index (NDI), Short Form 36 (SF-36), Modified Macnab criteria. The VAS score for pain was the only outcome measure used in all studies, except for one. However, it was not used in a consistent manner. An overview of the study characteristics is presented in Table 1.

Risk of Bias within Studies

Considering the method used for appraising the risk of bias within studies, all studies had a high risk of bias resulting in a low methodological quality, except two.[7,17] See Tables 2 and 3.

Results of Individual Studies

RCTs. A study by Nardi et al.[19] showed complete resolution of symptoms in 80% of all cases (n = 50) at 60 days after nucleoplasty compared with only 20% in the control group (CC, n = 20). Ten percent had no complete amelioration and remained under clinical FU with a wait-and-see prospective. The remaining 10% without any clinical improvement were treated with alternative traditional methods. Patients with complete resolution of symptoms returned to work after 21 days on average (range 15 to 36). Patients of the control group returned to work after 46 days (range 25 to 50). No complications were observed during the study. Overall, at short term, the nucleoplasty group significantly improved from baseline ($P \leq 0.001$), unlike the control group ($P = 0.172$). This study was appraised to be of low methodological quality.

Birnbaum[10] compared 26 PCN patients with a CC group (n = 30). The pain scores (VAS) in the PCN group were 8.8 (pre-operatively), 2.0 (3 months), 2.7 (6 months), and 2.3 (24 months), respectively. In the control group (n = 30), the VAS pain score improved from 8.4 (pre-operatively) to 5.1 (24 months). All patients in the PCN group returned to work between 24 hours and 2 weeks, with an average postoperative recovery period of 8 days. No complications were observed during the study. Although no statistical analyses were performed within this study, nucleoplasty showed lower VAS pain scores compared with conservative treatment at short-, mid-, and long-term FU. The methodological quality of this study was also low.

Cesaroni et al.[17] compared 62 patients treated with PCN to a CC group (n = 58). Main outcome measures were VAS pain score, NDI, and SF-36 quality of life score. The PCN group had significant lower VAS pain scores at all FU time points ($P < 0.0001$). The NDI also improved significantly at 6 weeks ($P < 0.0001$) and 1 year FU ($P = 0.005$), and correspondingly, the SF-36 physical component summary (PCS) improved significantly at 6 weeks ($P = 0.004$), 3 months ($P = 0.0237$), and 1 year FU ($P = 0.0003$). Moreover, a statistically higher percentage of PCN patients achieved the minimal clinically important difference (MCID) for VAS pain scores at 6 weeks ($P < 0.0001$), 3 months ($P = 0.01$), and 1 year FU ($P = 0.0003$), and for NDI scores only at final FU ($P = 0.002$) (Table 4). No complications were observed during the study. Overall, the statistical analyses favor nucleoplasty, mainly at

short- and longterm FU. This study was appraised to be of high methodological quality.

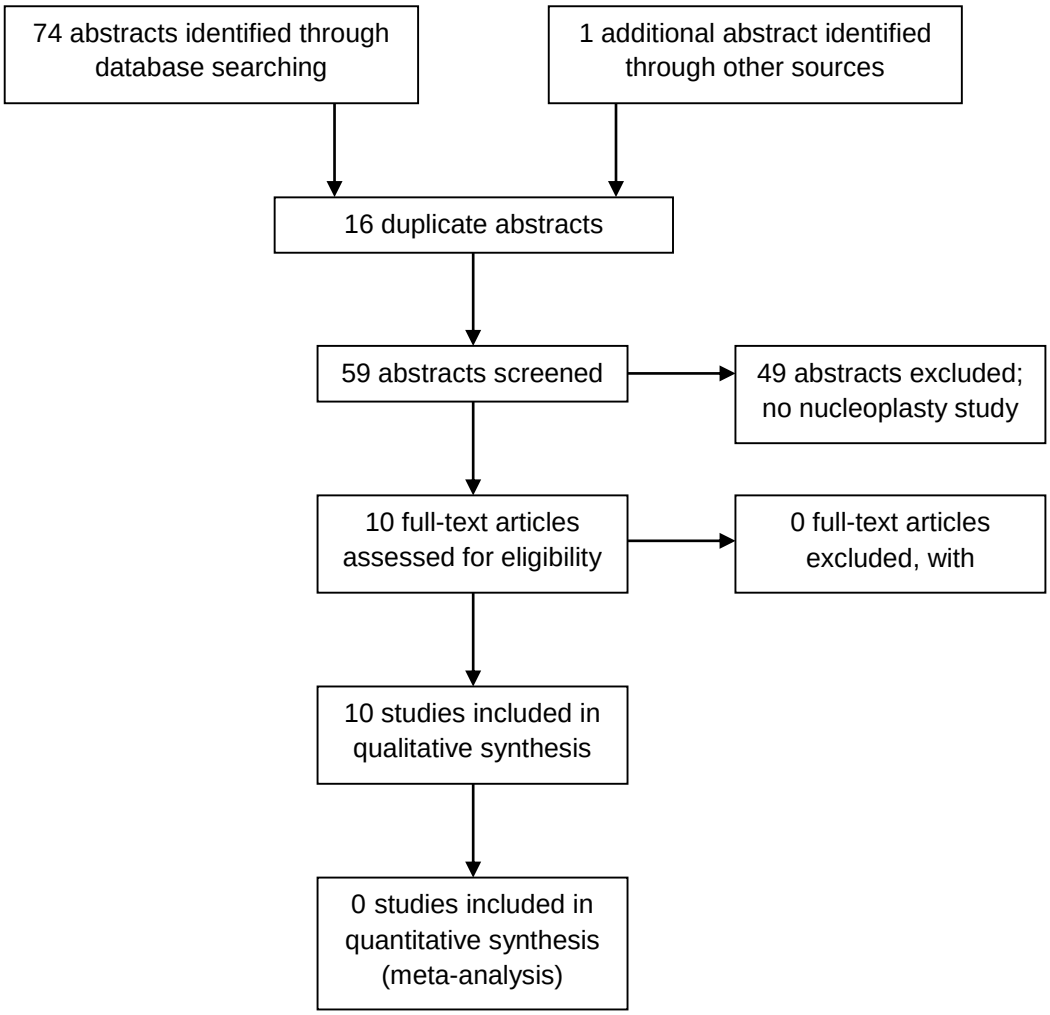

Figure 1. PRISMA flow diagram of the study selection

Table 1. Overview of the Study Characteristics

Author(s), Year	Study design	Treatment	Number of patients	Number of treated disk by PCN	FU term
Nardi et al., 2005[19]	RCT	PCN vs. CC	70 (50 PCN / 20 CC)	54 (46 unilevel, 4 multilevel/C4–C5, (12) C5–C6 (33), C6–C7 (9))	Up to 60 days postoperatively
Birnbaum, 2009[10]	RCT	PCN vs. CC	56 (26 PCN / 30 CC)	29 (23 unilevel, 3 multilevel/C4–C5, (8) C5–C6, (19) C6–C7 (2))	Preoperative, 1 day (only PCN group), 1 week, 1, 3, 6, 12, and 24 months postoperatively
Cesaroni et al., 2010[17]	RCT	PCN vs. CC	115 (62 PCN / 53 CC)	≥ 62, Not reported	Preoperative, 6 weeks, 3, 6, and 12 months postoperatively
Slipman et al. 2003[20]	Uncontrolled prospective case series	PCN	5 (all PCN)	5 (5 unilevel /C4–C5, (1) C5–C6, (2) C6–C7 (2))	Preoperative, 2, 4, 6 weeks, 3, and 6 months postoperatively
Bonaldi et al., 2006[21]	Uncontrolled prospective case series	PCN	55 (all PCN)	75 (36 unilevel, 19 multilevel/C4–C5, (5) C5–C6 (37), C6–C7 (33))	FU period 2 to 29 months, with results presented at 2 and 6 months FU
Li et al., 2008[9]	Uncontrolled prospective case series	PCN	126 (all PCN)	126 (126 unilevel / C3–C4, (21) C4–C5 (30), C5–C6 (40), C6–C7 (35))	Preoperative, 2 weeks, 1, 3, 6, and 12 months postoperatively
Azzazi et al., 2010[22]	Uncontrolled prospective study	PCN	47 (all PCN)	65 (30 unilevel, 17 multilevel/C4–C5, (14) C5–C6 (44), C6–C7 (7))	Preoperative, 1, 3, 6, 12, and 24 months postoperatively

Table 1, continued

Author(s), Year	FU term	Reported complications	Main outcome measure(s)	Study result(s)/Conclusion
Nardi et al., 2005[19]	Up to 60 days postoperatively	No complications were observed	VAS pain score diverted to good, poor and no result (percentages)	Significant improvement in percentage of patients treated with PCN ($P \leq 0.001$), while clinical resolution in the CC group was not always reached ($P = 0.172$)
Birnbaum, 2009[10]	Preoperative, 1 day (only PCN group), 1 week, 1, 3, 6, 12, and 24 months postoperatively	No complications were observed	VAS pain score	PCN showed better results than the continuation of CC
Cesaroni et al., 2010[17]	Preoperative, 6 weeks, 3, 6, and 12 months postoperatively	No complications were observed	VAS pain score; NDI; MCID based on VAS and NDI scores; SF-36	PCN offers improved pain relief as well as superior immediate and long-term gains in functional ability and quality of life when compared to CC
Slipman et al. 2003[20]	Preoperative, 2, 4, 6 weeks, 3, and 6 months postoperatively	Not reported	VAS pain score; Medication usage; Return to work rate	More than 75% reduction in VAS pain score was found at all FU intervals for each subject; 4 patients returned to work full time within 2 weeks, the fifth had secured early retirement
Bonaldi et al., 2006[21]	FU period 2 to 29 months, with results presented at 2 and 6 months FU	One case of infectious diskitis (treated successfully, but poor clinical outcome); One case with broken tip remained in disk space, asymptomatic during > 2 years	Modified Macnab criteria	PCN appeared to be a minimally invasive low-risk approach, which is easy to perform, associated with only minimal discomfort to the patient, and effective on the short-term
Li et al., 2008[9]	Preoperative, 2 weeks, 1, 3, 6, and 12 months postoperatively	One case with broken tip remained in disk space, but asymptomatic	VAS pain score; Modified Macnab criteria	PCN was shown to be an efficacious minimally invasive technique for the treatment of symptoms associated with contained cervical herniated disk
Azzazi et al., 2010[22]	Preoperative, 1, 3, 6, 12, and 24 months postoperatively	One case of diskitis (treated successfully, but persistent pain); One case with broken tip remained in disk space, but asymptomatic	VAS pain score; NDI	The use of PCN for the treatment of intradiskal herniation provided encouraging results owing to low morbidity and good clinical outcome soon after the procedure

Table 2. Methodological Quality of the RCTs

References	Random sequence generation (selection bias)	Allocation concealment (selection bias)	Blinding of participants and personnel (performance bias)	Blinding of outcome assessment (detection bias)	Incomplete outcome data (attrition bias)	Selective reporting (reporting bias)	Other bias
Nardi et al.,2005[19]	-	-	-	-	+	+	-
Birnbaum 2009 [10]	-	-	-	-	+	+	-
Cesaroni et al.,2010[17]	+	+	-	-	+	+	-

- high risk of bias; +, low risk of bias.

Table 3. Methodological Quality of the Nonrandomized Studies

	Selection				Comparability		Outcome		
Reference	Representativeness of the exposed cohort	Selection of the non-exposed cohort	Ascertainment of exposure	Outcome of interest was not present at start	Study controls for diagnosis	Study controls for any additional factor	Assessment of outcome	Follow-up was long enough for outcomes to occur	Adequacy of cohort follow-up
Slipman, et al. 2003 (21)	-	-	+	+	-	-	+	+	+
Bonaldi, et al. 2006 (22)	+	-	+	+	-	-	+	+	+
Li, et al. 2008 (9)	+	-	+	+	-	-	+	+	-
Azzazi, et al. 2010 (23)	+	-	+	+	-	-	+	+	-
Yan, et al. 2010 (7)	+	+	+	+	+	-	+	+	+
Cesaroni, et al. 2011 (19)	-	-	+	+	-	-	-	+	+
Sim, et al. 2011 (12)	+	-	+	+	-	-	+	+	+

-, high risk of bias; +, low risk of bias.

Table 4. Statistical Outcomes of Cesaroni et al.[17] Comparing PCN and CC per FU

Clinical outcome	6 weeks FU	3 months FU	6 months FU	1 year FU
VAS pain score	P < 0.0001	P < 0.0001	P < 0.0001	P < 0.0001
NDI	P < 0.0001	NS	NS	P = 0.005
SF-36 (PCS)	P = 0.004	P = 0.0237	NS	P = 0.0003
VAS MCID	P < 0.0001	P = 0.01	NS	P = 0.0003
NDI MCID	NS	NS	NS	P = 0.002

FU, follow-up; MCID, minimal clinically important difference; NDI, neck disability index; NS, not significant; SF-36 (PCS), short form-36 (physical component summary); VAS, visual analogue scale. All significant outcomes favor PCN over CC.

Nonrandomized Studies. Slipman et al.[20] reported results from 5 patients after PCN. The VAS pain score was reduced more than 75% at all FU intervals (2, 4, and 6 weeks, 3 and 6 months postprocedure) for each subject. Four of 5 patients returned to full-time work within 2 weeks. No statistical analysis was performed; however, the results suggest that PCN may lead to rapid and prolonged pain relief at short- and mid-term in patients with cervical radicular pain due to an acute focal protrusion. The methodological quality of this study was low.

Bonaldi et al.[21] showed good to excellent outcomes (Modified Macnab criteria) in 80% of the 55 patients suffering from cervical soft disk protrusion at 2 months FU. The success rate increased even further at 6 months to 85%. One clinically relevant complication of diskitis was reported but treated successfully. In another patient, there was an in situ rupture of the device tip; however, this patient remained asymptomatic. According to this study, PCN appears to be an effective and safe treatment at short- and mid-term. The methodological quality of this study was also low.

Li et al.[9] evaluated the prospective results of 126 PCN procedures for contained cervical disk herniation at 2 weeks, 1-, 3-, 6-, and 12-month FU. The VAS pain scores improved statistically (P < 0.01) for all FUs (range 2.42 ± 0.71 to 2.44 ± 0.71) compared with preoperative findings (7.25 ± 0.44). The rate of excellent and good results based on the modified Macnab criteria was 81.7%. Besides a technical complication (broken device tip) that was asymptomatic, no complications were reported. This study shows PCN to be safe and effective at short-, mid-, and long-term FU. The methodological quality of this study was appraised to be low.

Azzazi et al.[22] assessed the safety and clinical outcome after PCN in 47 patients with contained disk herniation or focal protrusion at 1, 3, 6, 12, and 24 months FU. The VAS pain score decreased statistically (P = 0.001) from 8.1 ± 1.4 pre-operatively to a VAS pain score between 0.6 ± 0.5 to 1.1 ± 0.9 postoperatively. Complete resolution of symptoms (VAS < 2.0) was found in 72% (1 month), 83% (3 months), 79% (6, 12, and 24 months). The NDI improved statistically (P = 0.001) from 80.5 ± 4.4 preoperatively to a NDI score between 4.2 ± 3.8 to 12.6 ± 8.1 postoperatively. Significant improvement based on the NDI was found in 63.8% of the patients at 1 month, 76.6% at 3 months, and 80.6% at 6 to 24 months. One postoperative complication was reported (diskitis) and treated, but pain persisted. Also, an intra-operative complication (broken device tip) occurred in another patient; however, this patient was asymptomatic. The study concludes that PCN in

patients with contained disk herniation or focal protrusion is safe and effective at short-, mid-, and long term. The methodological quality of this study was low.
Yan et al.[7] retrospectively compared clinical outcomes of 176 patients with symptomatic contained cervical disk herniation treated with PCN (n = 81) or PCD (n = 95) at a FU of 16–48 months. In the PCN group, the VAS pain score improved from 7.12 ± 1.13 to 2.74 ± 0.89 (P < 0.001) compared with 7.18 ± 1.09 to 2.71 ± 0.91 (P < 0.001) in the PCD group. There was no difference found in success rates (Modified Macnab criteria scoring excellent or good) between both groups, respectively, 77.8% (PCN) and 79.5% (PCD). A technical complication (broken device tip) occurred in 1 patient, but this person remained asymptomatic. One case of diskitis was reported within the PCD group. The results show that both methods are safe and have good long-term clinical outcomes. This study was of high methodological quality.
Cesaroni et al.[18] evaluated clinical outcomes of 349 patients with contained herniated cervical disk or focal protrusion treated by PCN. Outcomes were assessed immediately postoperatively at 3 months and then every year up to 5 years. At all time points, 50% to 60% of the patients had good results, 30% to 40% satisfactory results, and 5% to 10% showed no change. One postoperative complication occurred (diskitis), but the patient was treated successfully. This study shows PCN to be effective and safe in patients with contained herniated cervical disk or focal protrusion at short- and long-term FU. The methodological quality of this study was appraised to be low.
Finally, Simet al.[12] assessed the efficacy of PCN in 22 patients with cervical disk disorders. The VAS pain score decreased significantly (P < 0.05) from 9.3 ± 0.9 (preprocedure) to 3.7 ± 2.1 (1-month postoperative) and 3.4 ± 2.3 (6 months postoperative). Patient satisfaction (Modified Macnab criteria) at 6 months was good to excellent in 76% of the patients, fair in 14%, poor in 5%, and worse in 5%. No complications were observed. The study results demonstrate PCN to be a safe treatment of cervical disk disorder with good shortand mid-term clinical outcomes. The methodological quality of this study was low.

Synthesis of Results

A best-evidence synthesis was performed, because metaanalysis was not possible due to clinical heterogeneity between the included studies in this systematic review.

Risk of Bias Across Studies

Following the best-evidence synthesis, the level of evidence for the efficacy and safety of PCN in patients with a herniated disk, when compared to CC at short-, mid-, and long-term FU, appeared to be moderate in the included RCTs.

Additional Analysis

The appraisal of applicability and clinical relevance of the study results, as suggested by Malmivaara et al.,[16] showed differences between the 3 RCTs. Two studies[10,19] had a low applicability and clinical relevance, mainly due to a poorly described study population, control intervention, cointerventions, outcome measures, and analyses. The third study[17] showed moderate applicability and

clinical relevance, because information about the control intervention and cointerventions lacked (Table 5).

Discussion

Summary of Evidence

Three RCTs (n = 241) focusing on treatment of patients with a herniated disk were included in the primary analysis of this systematic review.[10,17,19] Two studies[10,19] had low methodological quality, due to a high risk of selection, performance, and detection bias. All 3 compared nucleoplasty (n = 138) with conservative treatment (n = 103) and showed better results for PCN at short-, mid-, and long term. This finding needs to be interpreted cautiously because of the moderate quality of evidence, and low to moderate applicability, and clinical relevance of the study results.

As the number of available RCTs was very limited, nonrandomized studies were also included to broaden the extent of evidence on the efficacy and safety of PCN in patients with a herniated disk. Seven nonrandomized studies (n = 780) were included, reporting ≥ 747 disks treated by PCN.[7,9,12,18,20–22] Although 6 out of 7 had a high risk of bias, all 7 concluded that PCN was effective and safe for the treatment of a cervical herniated disk, thereby confirming the short-, mid-, and long-term results found in the primary analysis of RCTs. According to the nonrandomized studies, satisfactory or good to excellent results were found in ≥ 77.3% of the treated patients at final FU ranging from 6 to 60 months.[7,9,12,18,20–22] VAS pain scores decreased from 7.1 to 9.3 pre-operatively to 2.4 at 3 months, 2.4 to 3.4 at 6 months, 2.4 at 12 months, and 2.7 at 16 to 48 months.[7,9,12] The NDI significantly improved in 63.8% of the patients at 1 month and 76.6% at 3 months FU.[22]

For the safety assessment of PCN, it is important to evaluate as much treated disks as possible. In this review, the total of both the RCTs (≥ 145) and nonrandomized studies (≥ 747) is ≥ 892. As complications were not explicitly reported in all studies, 1 study was excluded,20 remaining ≥ 887 PCN treated disks. Besides observed local anesthetic-related side effects, soreness at the needle insertion site, new numbness and tingling, increased intensity of preprocedure pain and new areas of pain, 4 cases of diskitis were reported.[7,18,21,22] These complications were treated successfully in 3 patients. The treatment results of 1 complication were not reported. Four successfully treated cases reported a broken tip of the device that remained in the intervertebral disk, without causing any complications.[7,9,21,22] Although this number is very low, it should be considered an avoidable complication by improving used materials.

Based on these figures, PCN seems to be a safe technique.

Table 5. Appraisal of Applicability and Clinical Relevance of the RCTs

Items	Nardi et al., 2005[20]	Birnbaum 2009[10]	Cesaroni et al., 2010[18]
Methods: Does the report enable the assessment of applicability?			
Study population	-	+	+
1 Age	-	+	+
2 Gender	-	-	+
3 Setting	+	+	+
4 Type of disease/disorder	+	+	+
5 Duration of disease/disorder	+/-	+	+
6 Severity of disease/disorder	-	-	+
7 Recruitment procedure	+	+/-	+
8 Description of inclusion and exclusion criteria			
Index intervention			
9 Type/content	+	+	+
10 Intensity/dosage	+	+	+/-
11 Frequency	+	+	+
12 Duration	+	+	+
13 Experience of provider	-	-	-
14 Proper intervention to answer the research question	+	+	+
Comparator (control intervention)			
15 Type/content	+	+	+
16 Intensity/dosage	+/-	-	-
17 Frequency	+/-	-	-
18 Duration	+/-	-	-
19 Experience of provider	-	-	-
20 Proper intervention to answer the research question	+	+/-	+
Cointerventions per study group			
21 Type/content	+/-	+/-	+
22 Intensity/dosage	-	+/-	-
23 Frequency	-	-	-
24 Duration	-	-	-
25 Experience of provider	-	-	-
Outcome measures			
26 Main symptom, disease-specific disability, and generic	+/-	+/-	+
disability	+/-	+/-	+
27 Validity and reliability of instruments	+	+	+
28 Follow-up moment	+/-	+/-	-
29 All potential adverse effects			
Analysis			
30 Intention-to-treat analysis	-	-	+
31 Confounding considered	-	+/-	+
32 Effect modification considered	-	+/-	+
33 Economic evaluation	-	-	-
Results: Are the study results clinically relevant?			
34 Baseline values of main symptoms and disability plus	-	+/-	-
measure of variance	+	+/-	-
35 Adherence in all study groups	+	+	+
36 Dropout rate	-	+/-	+
37 Follow-up values of main symptoms and disability plus	-	-	-
measure of variance	-	+/-	+
38 Confidence intervals of between-group differences	+	-	+
39 Magnitude of difference between groups			
40 Incidence of all adverse			

- no; + yes; +/- not clear.

As available literature on PCN-treating disk herniations is limited, we also compared reported results with the most recent systematic review on the effectiveness of lumbar nucleoplasty for treating contained disk herniation.[8] They found VAS pain scores at baseline of ± 7.1 and ± 4.0 at 1, 3, 6, and 12 months FU. Successful outcomes, defined as more than 50% pain relief or a 2-point reduction on VAS, were found in 62.1% of the patients on average (range 6.25% to 84%).[8] No major complications were reported related to nucleoplasty.[8] Based on these figures, safety is comparable, but PCN seems to be more effective, as already proposed by Sim et al.[12] However, a clear explanation is lacking, and the quality of evidence in the analyzed studies was moderate.[12]

An important factor in the success rate of nucleoplasty lies in its technique. The basic mechanism of percutaneous disk decompression has been well understood. The removal of approximately 1 mL of disk tissue volume, corresponds to a diskal volume reduction of about 10% to 20% and a disproportionately large fall (> 95%) in intradiskal pressure,[7–9,23–25] which in turn reduces some chemical and mechanical factors causing pain.[8] However, several techniques exist, and each method has its own limitations like removal of too much tissue, indiscriminate removal of tissue, thermal injury to the disk or aggressive access into the disk.[10,12,26] Nucleoplasty using Coblation technology claims to be not affected by these limitations. It removes a portion of the nucleus tissue using a one-millimeter-diameter bipolar instrument that creates radio frequency energy.[8] Ablation is accomplished with a low-temperature (typically 40 to 70°C) plasma field of ionized particles, rather than heat.[2,8,11,25,26] These particles have sufficient energy to break down organic molecular bonds within the tissue, dissolving the soft tissue material of the disk nucleus.[2,8,11,25] Therefore, the technology provides simple, efficient disk decompression, because of controlled and highly localized ablation, resulting in minimal damage to surrounding healthy tissue.[2,8–11] Considerable studies have also noted the importance of application in well-selected cases, mainly resulting from the technical background.[8,10,12,22] For example, patients with a contained herniated disk and minimally degenerated disks confirmed on MRI, who are unresponsive to conservative treatment and suffering more arm than axial neck pain.[8,10,12]

A meta-analysis was not possible because of clinical heterogeneity between studies. The VAS pain score was the main outcome in all trials but used in an inconsistent manner. The included studies had different FU terms, number of patients treated and, whether or not applicable, different alternative treatment courses. Nonetheless, all authors concluded PCN to be a safe, promising, and efficacious procedure for symptomatic (contained) disk herniation.[7,9,10,12,17–22] However, the best-evidence synthesis of the analyzed RCTs (study design that ranks second highest on the evidence ladder) showed only a moderate quality of evidence for the effectiveness of PCN compared with CC at short-, mid-, and long-term FU. Based on this result, we conclude the effectiveness of PCN in patients with a herniated disk to remain uncertain and its application doubted. In addition, the included RCTs had only low to moderate applicability and clinical relevance of study results, mainly due to poorly described study population, control intervention, cointerventions, outcome measures and analysis within their study reports. As a result, the transfer of study outcomes to general daily practice is currently limited. Therefore, it is not only very important to increase the number of studies investigating PCN, but also to improve the methodological quality and level of

evidence, and the reporting of RCTs including their results. Besides CC, minimally invasive methods (ie, pulsed radiofrequency) should be compared too.

Limitations

As PCN in patients with a cervical herniated disk is relatively new and still considered controversial, available literature is limited.[5,13] Only 3 RCTs and 7 nonrandomized studies were included. Due to clinical heterogeneity, a meta-analysis was not possible. However, we were able to discuss and compare the analyzed studies and to provide a best-evidence synthesis of the RCTs included in the primary analysis,[5,16] while appraisal of the applicability and clinical relevance of these studies was carried out as a valuable, additional analysis. To improve the reporting of our systematic review, the PRISMA statement was used.[27]

Conclusions

All included studies show PCN to be an effective and safe procedure in the treatment of (contained) herniated disks at short-, mid-, and long term FU. However, the level of evidence is moderate, because the majority of reviewed studies have a nonrandomized design, and moreover, the identified RCTs are in general of poor methodological quality and show only low to moderate applicability and clinical relevance. Although the primary outcomes are promising and the application of PCN is encouraged in well-selected cases, more and better-designed studies using validated outcome measures are needed.

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Chapter 7

Percutaneous Cervical Nucleoplasty vs. Pulsed Radio Frequency of the Dorsal Root Ganglion in Patients with Contained Cervical Disk Herniation; A Prospective, Randomized Controlled Trial

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Abstract

Background: Cervical neck pain is often caused by cervical disk pathology and may cause severe symptoms and disability. Surgeons and patients are increasingly aware of postsurgery-related complications. This stimulated the clinical usage of minimally invasive treatments such as percutaneous nucleoplasty (PCN) and pulsed radio frequency (PRF). However, scientific evidence on both treatments is limited.

Objective: Our objective was to evaluate the efficacy of PCN compared to PRF in patients with contained cervical disk herniation.

Methods: A prospective randomized clinical trial was conducted including 34 patients with radicular pain due to a single contained cervical disk herniation who were treated with either PCN or PRF. Demographic data were collected, and the Medical Outcomes Study 12-Item Short Form (SF-12) Health Survey, visual analog scale (VAS), and the Neck Disability Index (NDI) were completed 1, 2, and 3 months after treatment. Treatment satisfaction and complications were recorded.

Results: In the PCN group (n = 17, mean age 52.4 years, 10 female/7 male), patients were treated at C5 to C6 (8 cases) or C6 to C7 (9 cases). In the PRF group (n = 17, mean age 49.5 years, 8 female/9 male), patients were treated at C3 to C4 (1 case), C5 to C6 (10 cases), or C6 to C7 (6 cases). At 3 months, mean pain VAS improved significantly from baseline in the PCN group (mean improvement: 43.4 points) and in the PRF group (34.0 points). However, improvement in 1 group was not superior compared to the other group (P = 0.48). No serious complications were reported.

Conclusion: Within 3 months, both PCN and PRF show significant pain improvement in patients with contained cervical disk herniation, but none is superior to the other. Both treatment options appear to be effective and safe in regular clinical practice.

Introduction

Neck pain caused by cervical disk pathology may cause severe symptoms and disability.[1] It is also difficult to treat and a costly healthcare issue.[2] Approximately 1 person in 1,000 suffers from cervical radicular pain.[3,4] Treatment options are conservative at first, but more severe or resistant cases need surgical intervention.[5] Examples of conservative care are rest, physiotherapy, and oral medication. If conservative treatment fails, percutaneous, minimally invasive (radiological) procedures can be used to relieve pain.[1] These procedures work by minimizing pressure or chemical irritation on sensory nerves, while at the same time minimizing trauma to healthy tissues.[6–8] Although different minimally invasive treatment modalities are described in the literature, scientific evidence on their effectiveness is limited, making it difficult for the clinician to decide which treatment modality should be used.[3,5] The current trends in spinal surgery are nowadays reducing surgery related trauma, increasing patients' awareness of alternatives to surgical procedures and development of new technologies (eg, percutaneous nucleoplasty [PCN]).

The basic principle of most percutaneous procedures is that a small volume reduction in approximately 1 mL in a hydraulic space, such as a healthy spinal disk, results in a volume reduction of about 10% to 20%[7–9] with a subsequent large pressure decrease. This decreased pressure may result in relief of chemical and mechanical factors which cause symptoms such as pain and sensory or motor function loss.[8] PCN is a percutaneous disk decompression (PDD) technique using coblation technology (Figure 1A,B).[6] With a 1mm diameter bipolar instrument, which creates radio frequent energy, a low temperature (typically 40 to 70°C) plasma field of ionized particles removes some nucleus tissue.[6] These ionized particles are able to break down organic molecular bonds thereby dissolving part of the disk nucleus.[2] While the basic mechanism of percutaneous disk decompression (PDD) has been well understood, there are concerns on indiscrete removal or removal of too much tissue,[10,11] although several studies have shown that PCN is both safe and effective.[1,6–12] Clinically, PCN is the most often used treatment for patients with a herniated cervical disk.[1]

Pulsed radio frequency (PRF) treatment of the dorsal root ganglion is also an acknowledged pain treatment modality for (cervicogenic) disk pain. It is used as a minimally neurodestructive technique, as an alternative to radio frequency heat lesions, with significantly fewer complications.[13,14] Radiofrequency treatment of the cervical dorsal root ganglion (DRG) to treat cervical radicular pain was first described by van Kleef et al.,[8] but because of reported side effects and the possibility of deafferentation pain, PRF is now commonly accepted for cervical DRG treatment (Figure 2A,B). Van Zundert et al.[3] concluded that PRF treatment had significantly better outcomes compared to sham treatment.

Both PCN and PRF are applied in clinical practice with promising results; however, studies comparing the effectiveness of both interventions are lacking.[5] In this study, we prospectively studied the effectiveness of PCN vs. PRF in patients with a contained cervical disk herniation. As PCN is a causal therapy in contrast to the symptomatic PRF treatment, we hypothesized that PCN would result in superior clinical outcomes compared to PRF.

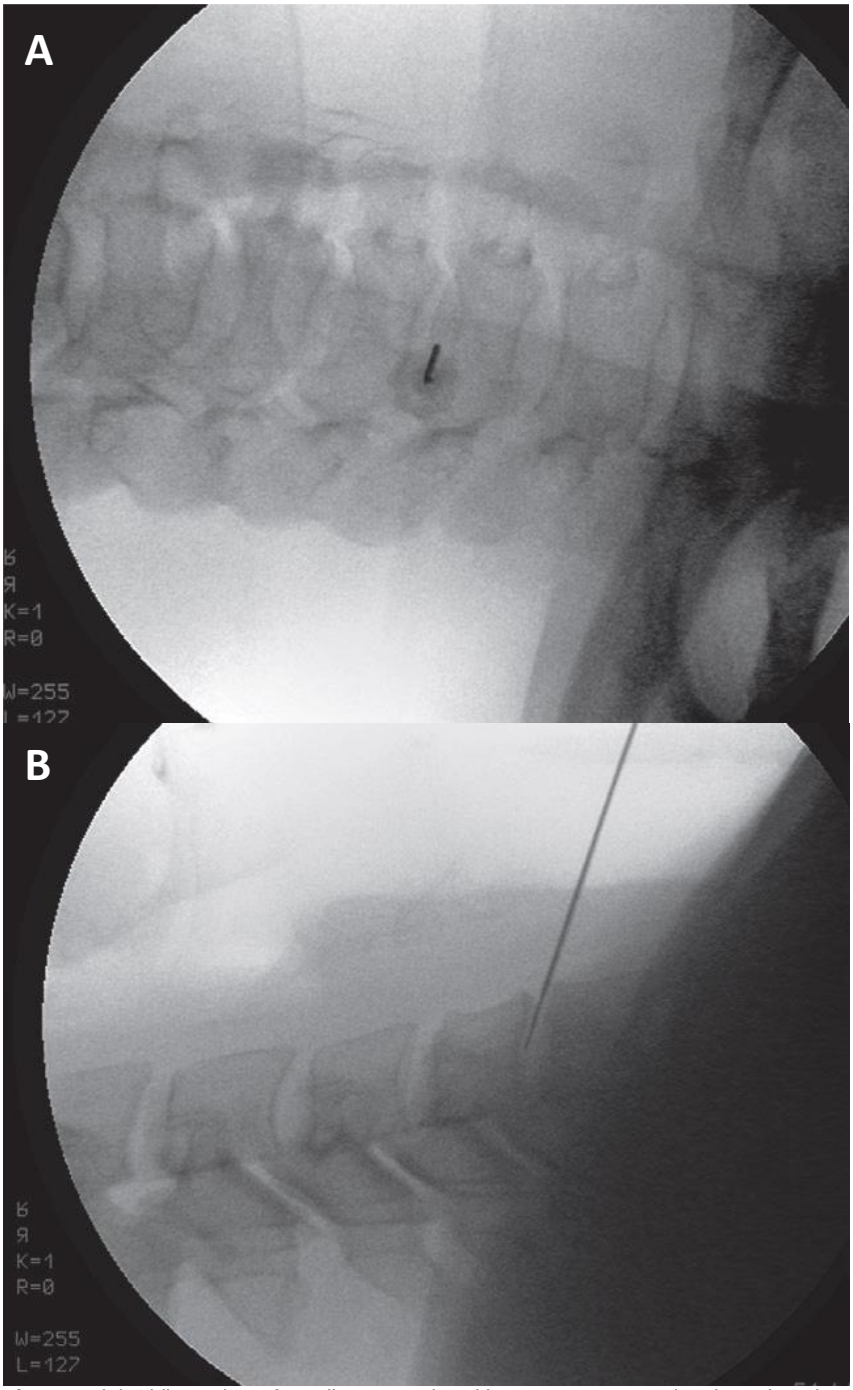

Figure 1. (A) Oblique view of needle entry point with percutaneous nucleoplasty (PCN) treatment (C5 to C6 level). (B) Lateral view of needle depth with PCN treatment (C5 to C6 level).

Methods

Patient Population

In this prospective, randomized controlled study, 38 patients (Table 1) with single-level contained cervical disk herniation confirmed on prestudy clinical MRI were, after providing written informed consent, included and randomized to either percutaneous nucleoplasty treatment (PCN group) or pulsed radiofrequency treatment (PRF group) (Figure 3). Patients were seen after the neurologist diagnosed a disk herniation using MRI and history taking. Our study was approved by the Medical Review Board (nr. NL39783.015.12). We included patients with a contained, single-level cervical disk herniation diagnosed on recent MRI (< 4 weeks), who failed conservative treatment and reported radicular pain (≥ 50 mm on 100 mm Visual Analogue Scale for pain [VAS- 100 mm]) with or without neck pain corresponding to the herniated level, and a disk height over 50% of adjacent level. No electromyographical examination was performed, but patients who did not respond (> 50% temporary pain relief for at least 30 minutes) to a diagnostic nerve block[15] placed with local anesthetic (Lidocaine 1% 1 mL) at the level identified with history taking and MRI (Figure 4A,B) were excluded. Patients with extruded disk fragmentation, cervical spondylolisthesis, or spinal canal stenosis and patients with previous surgery at the index cervical disk herniaton level were also excluded. All remaining patients were consequently randomized.

Description of the Performed Interventional Techniques

PCN Treatment. Before entering the operating room, 1,000 mL of NaCl solution was administered to the patient. Cefazolin (1.0 g) was intravenously injected as antibiotic prophylactixis, with continuous vital sign monitoring and oxygen supply at 5 L/min via nasal prong during the procedure. The procedure was performed under local anesthesia, but propofol was administered in increments for sedation. To make access into the desired cervical disk possible using the standard rightsided anterolateral approach, the patient was placed in a supine position, arms next to the body and the neck slightly hyperextended. A chlorhexidine solution was applied for disinfecting the anterior neck area including the surrounding skin, and sterilized drapes covered the operating area. The percutaneous cervical nucleoplasty procedure was performed using C-arm fluoroscopic imaging (Ziehm, Vista, Orlando, FL, U.S.A).

First, the position and angle of the targeted disk were visualized radiographically. Anteroposterior and caudal angulation was used to optimally visualize the disk space; oblique rotation was used to get a view in which the trachea/esophagus is outside the center of the beam. Based on these images, the entry point for the needle was marked next to the medial border of the right sternocleidomastoid muscle. After marking the entry point, local anesthetic (1% lidocaine) was applied in the space between 2 fingers to anesthetize the skin and subcutis. One finger was positioned at the lateral border of the trachea and larynx, and the other pushed the carotid artery away and pointed toward the vertebral surface. It was important to check that no blood was aspirated with repeated suction and injection.

To confirm that the needle was introduced correctly, repeated suction and injection was used to check there was no aspiration of blood.

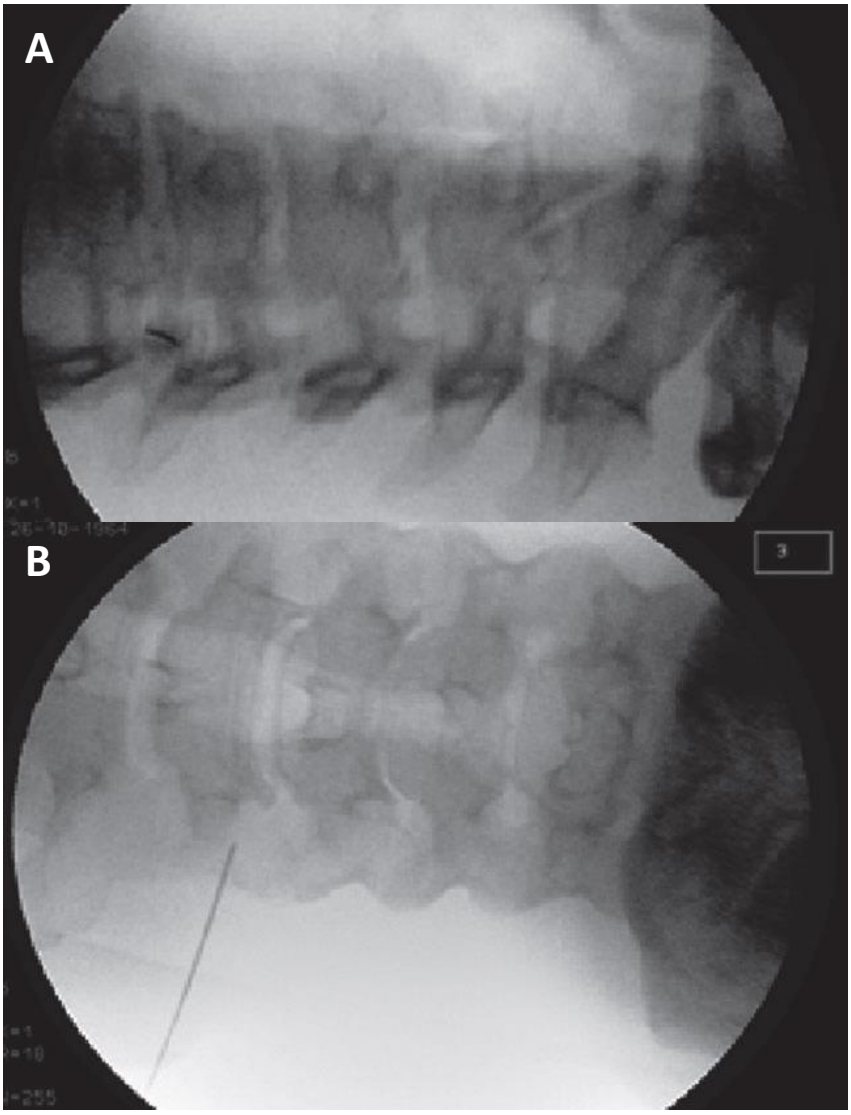

Figure 2. (A) Pulsed radio frequency (PRF) treatment C6 level, oblique view of needle positioning. (B) PRF treatment C6 level, anterior–posterior (AP) view for needle depth assessment.

Table 1. Patient Population Characteristics

		PCN	PRF	*P*
Male/female		7/10	9/8	0.37
Mean age (years)		52.4	49.5	0.74
Duration of symptoms (months)		11.9	12.1	0.95
Level of herniated disk	C3/4	0	1	n/a
	C5/6	8	10	n/a
	C6/7	9	6	n/a

PCN, percutaneous nucleoplasty; PRF, pulsed radio frequency.

Next, a 19-gauge trocar 3-inch spine needle (ArthroCare Co., Sunnyvale, CA, U.S.A.) was brought to the annulus fibrosis of the herniated disk. C-arm fluoroscopic images in anteroposterior, oblique, and lateral planes were made to control the direction of the needle in regard to the disk surface and confirm its end position. If in the correct position, the stylet was withdrawn and the Perc DC SpineWand (ArthroCare Co.) was introduced. After advancing slightly more and rechecking the final position, the standard ArthroCare power generator was connected. Before starting the procedure, 1 test was executed by coagulation. When no pain was remarked by the patient, the procedure could be performed safely. A short initial coagulation was performed when the wand was inserted, using 3 ablation cycles of 8 seconds each, and rotating the tip of the wand 180° when withdrawal was started with the control set at 125 V, causing a 52°C thermal reaction.[11] After withdrawing the needle slightly, coblation was repeated. Next, the trocar was removed and a skin plaster was applied. For the first 2 hours after the procedure, patients had to stay in bed in a supine position. They also were instructed to wear a cervical brace for 3 days, preventing uncontrolled movements of the cervical spine. Patients were discharged with postoperative precaution instructions and contact numbers in case of complications. A follow-up visit at the outpatient clinic was scheduled 2 months after the procedure. The cervical nucleoplasty procedures were offered by 2 different experienced pain physicians.

PRF Treatment. With PRF, the nerve is exposed to a high-frequency electric field with a maximal temperature of the electrode tip of 42°C. All PRF treatments were performed in the outpatient treatment room. After positioning the patient supine, the entry point was located using C-arm fluoroscopy. Next, the skin at the entry point was decontaminated using an alcohol swab and a 21-gauge 5-cm long Cosman (type CC) needle with a 5-mm active tip was inserted under fluoroscopy. An oblique view tunnel vision to the dorsocaudal of the foramen at the treatment level was used for optimal needle placement. When correct needle direction was confirmed with fluoroscopy, the C-arm was moved to an anterior–posterior (AP) view for determining correct needle depth. When both correct direction and depth were reached, a 50 Hz sensory stimulus was applied, which was confirmed by the patient targeting a 0.4 V. Next, a 2 Hz motor stimulus was used and confirmed by the patient to make sure the correct cervical level was targeted. After confirming the sensory and motor stimulus, a 45 V, 2 Hz (20 ms) PRF stimulus (maximum of 42°C) was applied for 6 minutes. After the PRF stimulus was completed, the needle was withdrawn and the skin covered with a standard skin plaster. For precautions, the patient was observed for 30 minutes before being discharged home.

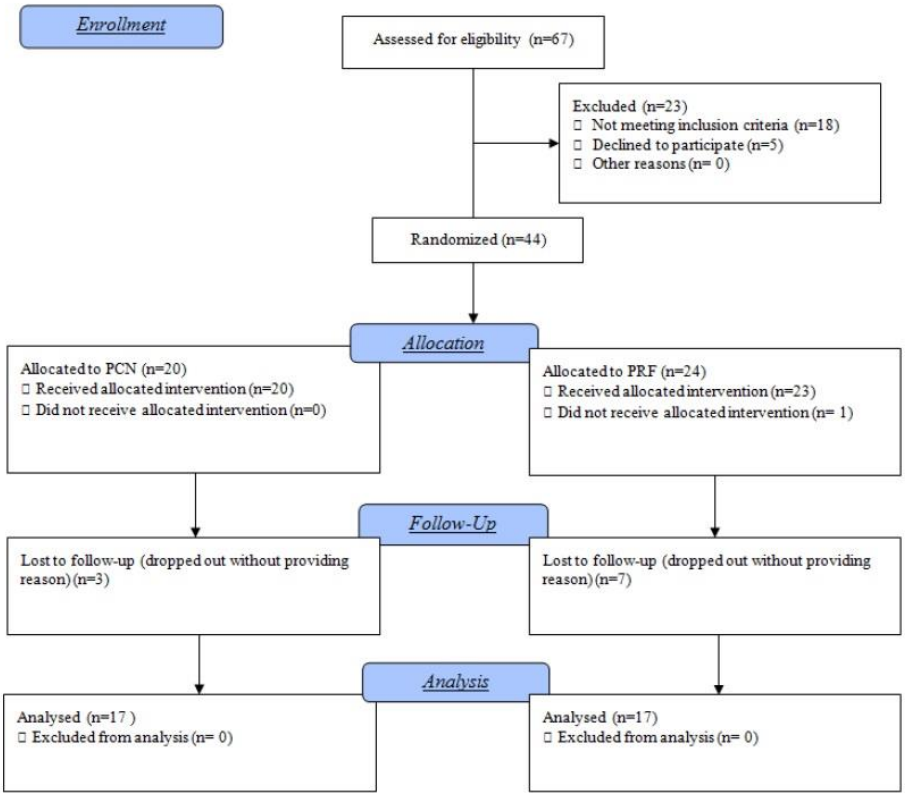

Figure 3. Consort 2010 study flow diagram.

Rehabilitation Procedure

Rehabilitation procedures were equal for both treatment groups. Patients were allowed to continue their own medication and gradually return to their previous activity level. Within the first 2 days, patients were not allowed to lift anything, to bend over, or to drive a car. They were also not allowed to sit for longer than 10 to 20 minutes or walk longer than 20 minutes continuously. Between day 2 and 14, patients were allowed to start with light activities, lifting no more than 5 kg, gradually increasing walking distance to 2 times for a half an hour per day. After 1 week, they were also allowed to start cycling for half an hour maximally. Turning the head quickly was prohibited during the first week. Until 2 weeks, swimming or being treated by a chiropractor or a manual therapist was not allowed. After 2 to 4 weeks, patients were allowed to resume their work, to start bending and cervical stretching, and to resume swimming. Increasing walking activities to 1 hour continuously per day was allowed. However, lifting more than 15 kg was not allowed for the first 6 weeks. After 4 weeks, patients were allowed to start their rehabilitation program under supervision of a physical therapist.

Clinical Follow-up

Clinical improvement for both treatment groups was assessed with a Visual Analogue Scale-100 mm (VAS) for pain change,[16] a 4-level item for pain improvement and a 4-level item for patient satisfaction combined with a VAS for satisfaction. Furthermore, neck and limb functioning and quality of life were measured with the Neck Disability Index (NDI) which scores 0 (best) to 50 (worst)[17] and the Short Form 36 (SF-36).[18] Also the number, nature, and severity of complications, use of pain medication pre- and postoperatively, and recurrence of symptoms/cases were recorded.

Statistical Analyses

The data are presented as mean ± SD. Outliers were filtered out by checking if all data were in the range of mean ± 2 SD. Descriptive statistics were used to present the results of the main variables. In case of normal distributed data, a 2-sided Student's t-test for independent samples was used to compare mean VAS pain and mean VAS satisfaction. When the between-groups analysis resulted to be significant, a post hoc analysis was executed within groups. The level of statistical significance was set at $P < 0.05$. For all statistical analyses SPSS (version 19.0) was used.

The sample size calculation was based on the difference in mean VAS (0 to 100 mm) scores for pain between groups at 3 months. The minimally clinical important difference (MCID) was set at ≥ 20 mm at the last follow-up based upon published literature. Power analysis (PS—Power and Sample Size Calculation; Informer Technologies Inc., Madrid, Spain), assuming a SD of 15 mm, using a significance level of 0.05 and a power of 90% resulted in a sample size of 15 patients per group.

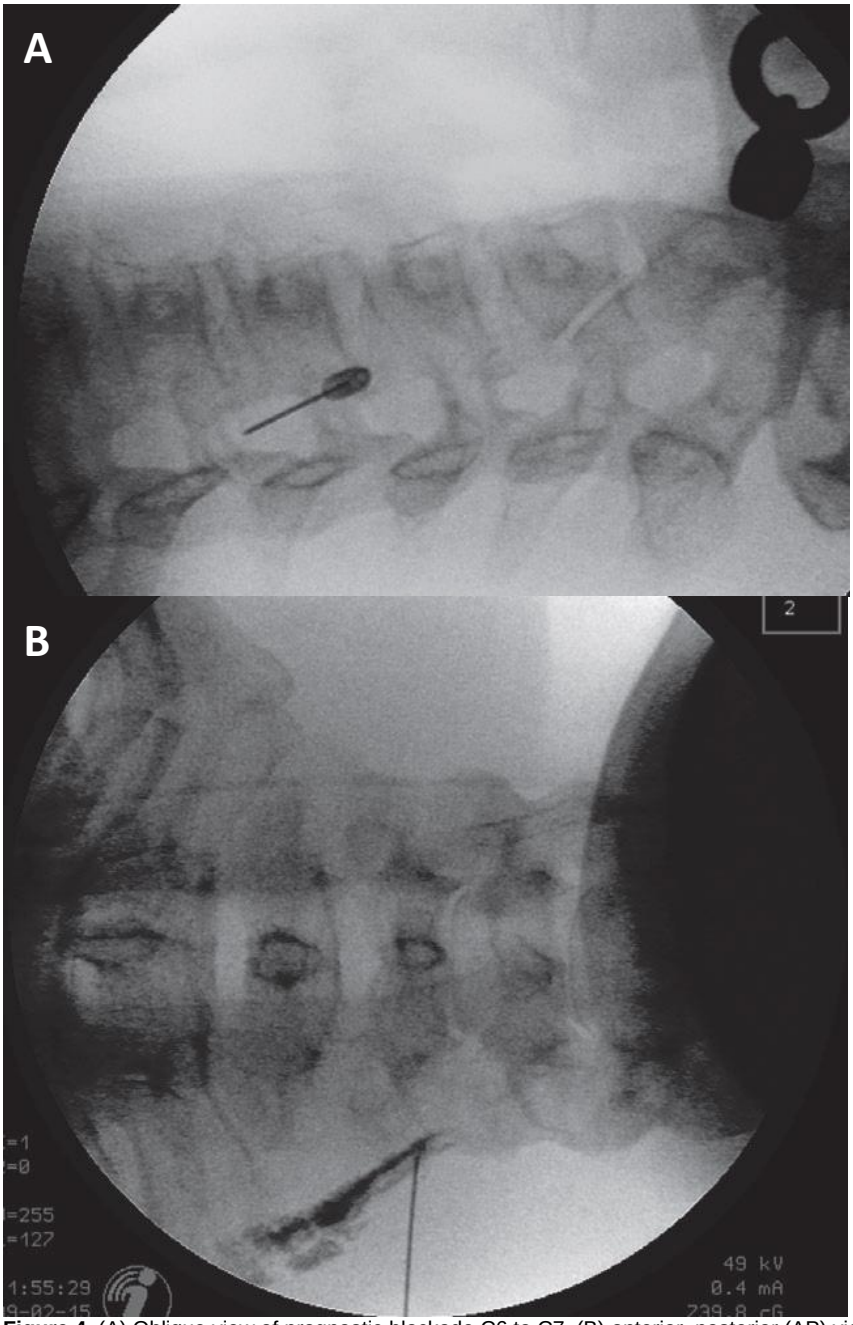

Figure 4. (A) Oblique view of prognostic blockade C6 to C7. (B) anterior–posterior (AP) view of prognostic blockade C6 to C7 with contrast.

Results

Treatment Results

In both groups, mean VAS pain scores improved at each follow-up time point compared to baseline (Figure 5). Eleven patients were lost to follow up. At 3 months follow-up, mean VAS pain improved 43.4 points in the PCN group vs. 34.0 points in the PRF group (P = 0.48). Mean VAS pain scores showed more improvement in the PCN group compared to the PRF group at each time point, but this difference never reached statistical significance (Table 2). There were 65% responders in the PCN group (11/17) compared to 53% responders in the PRF group (9/17, P = 0.49). Patient satisfaction with treatment results (VAS score) in the PCN group was 58.4 compared to 63.5 in the PRF group (P = 0.69).

Complications

There were no serious complications, but 3 patients in the PCN group and 3 patients in the PRF group reported minor side effects. In the PCN group, all complications were transient and mostly localized in the neck area, consisting of problems with swallowing. In the PCN-treated patients, no postoperative discitis occurred. In the PRF group, complications were mainly noticed outside the neck region, which consisted of headaches and muscle stiffness, and were also transient. All complications were mild in severity.

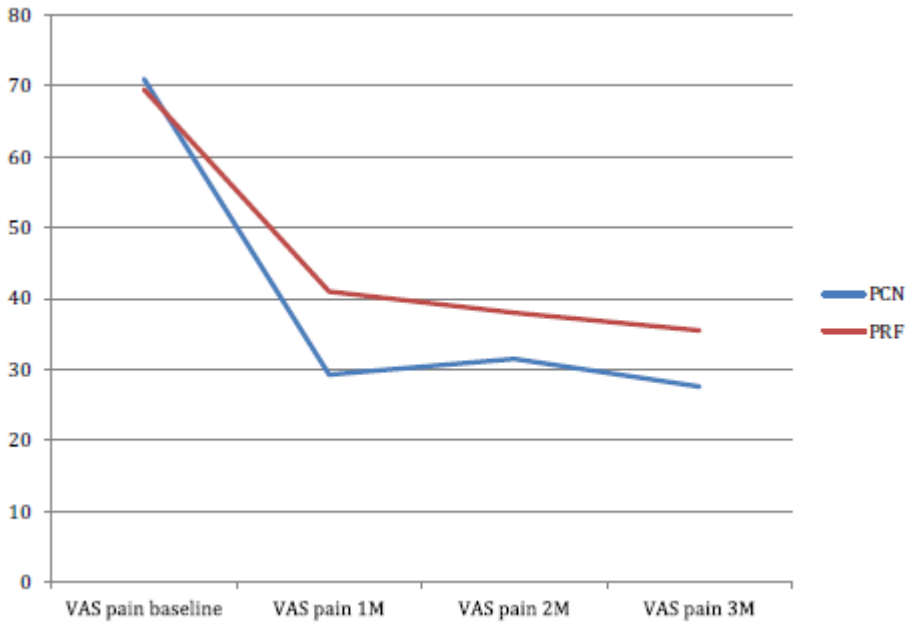

Figure 5. Visual analog scale (VAS) pain results at each follow-up point.

Table 2. Main Study Outcomes at Each Follow-Up

	PCN (n = 17)	PRF (n = 17)	*P*
VAS pain			
Baseline	71.0	69.5	0.75
1M	29.3	41.0	0.26
2M	31.5	38.0	0.55
3M	27.6	35.5	0.48
NDI			
Baseline	21.1	19.4	0.54
1M	15.9	14.9	0.84
2M	12.3	12.2	0.99
3M	11.1	10.8	0.93
VAS satisfaction			
1M	68.9	52.8	0.13
2M	67.8	60.9	0.55
3M	58.4	63.5	0.69

PCN, percutaneous nucleoplasty; PRF, pulsed radio frequency; VAS, visual analog scale; NDI, neck disability index.

Discussion

In this study, we compared 2 active treatments (PCN and PRF), rather than a placebo control or “usual care” comparison. In this prospective randomized controlled trial, there was no significant difference in outcome between PCN and PRF treatment for patients with a contained, single-level herniated cervical disk. However, with both procedures, VAS pain scores significantly improved after treatment compared to VAS pain scores before treatment. There was a trend for faster and more pain improvement using PCN treatment compared to PRF, but this difference failed to reach statistical significance nor did it reach a clinically important difference (mean reduction in VAS of > 30.0 mm).[19]

Currently, most published studies on the effectiveness of either PCN or PRF are retrospective in nature, limited in the number of included patients, do not use a control group, and usually include only lumbar disk herniation patients. Although cervical disk herniation is not observed as often as lumbar disk herniation, it is an important cause of neck pain resulting in severe symptoms and disability.[1] Patients with contained cervical disk herniation go through a variety of conservative treatments (eg, medication, fysiotherapy, manual therapy, epidural injection). Most of conservative treatments are not specific and take a longer time to recover and to regain quality of life. Surgical treatments range from cervical discectomy to artificial cervical disk replacement, or minimal invasive techniques such as PCN or PRF. Where discectomy or artificial disk replacement are more extensive, surgeries with consequently more adjacent risks are involved.[20] Percutaneous techniques such as PCN or PRF, in theory, involve less risk for the patient.

The advantage of PCN is that the procedure provides simple and efficient disk decompression with highly localized ablation causing minimal damage to surrounding tissue[2,4,6] (Figure 6A,B).

Similar to the results of Yang et al.,[21] who in a retrospective study analyzed 171 cervical disk herniation patients treated with either percutaneous cervical discectomy (97 cases), cervical PCN (50 cases), or a combination of these 2 treatments (24 cases), we found no differences in clinical outcomes between the treatment modalities. Yang et al. concluded that each of the 3 interventions they

studied was clinically effective and that PCN was the least invasive treatment option, but that costs for PCN were high. Sim et al.,[10] also in a retrospective study of cervical disk herniation patients (n = 22), concluded that PCN was safe and minimally invasive with excellent short-term clinical outcomes at 6 months which were similar to our 3-month results.

A recent study by Cahana et al.[13] reported that the biological effect of PRF was unlikely related to thermal damage, but that it was selectively targeting small diameter C and Ad nociceptive fibers. PRF should be considered nondestructive with very limited risk of (neurologic) complications. In a retrospective study, Yoon et al.[22] analyzed the results of PRF treatment for cervicogenic discus pathology (n = 22) and found a comparable improvement in pain scores (using a numeric rating scale) from baseline (mean NRS pain score 7) for up to 3 months after treatment (mean NRS score 2.5) as was observed in our study. In contrast to our results, they observed no complications related to PRF during the follow-up period. Chao et al.[23] retrospectively included a 165 patients treated with PRF for cervical (n = 49) or lumbar radicular pain (n = 116) and concluded that PRF was a safe and useful treatment, with no complications reported.

In our study, there were no differences in outcomes between PCN and PRF, indicating that both techniques can be considered equally effective. When choosing 1 treatment over the other, one should consider, for example, the complication risks, duration and treatment costs, the burden on the patient, and the experience of the treating physician with either of these procedures. Another consideration might be that PCN is a more causal treatment for discogenic herniation, as the herniation of the disk is retracted to the original space, where PRF is only symptomatic. Data on recurrence of symptoms are, however, unknown. Moreover, costeffectiveness concerning these treatments of cervical discogenic pain should be analyzed.

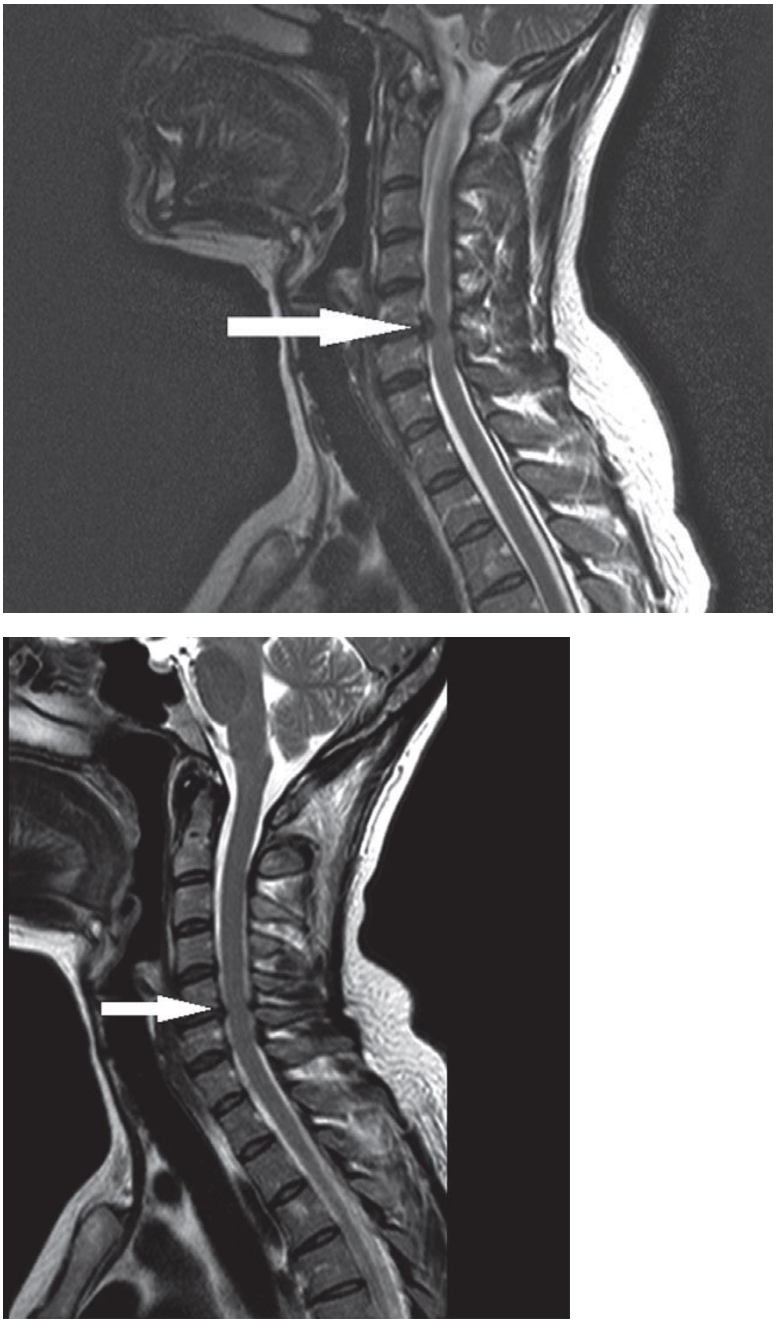

Figure 6. (A) Longitudinaal MRI of herniated disk at C5 to C6 level before percutaneous nucleoplasty (PCN) treatment. (B) Longitudinaal MRI of herniated disk at C5 to C6 level after PCN treatment.

Strengths and Limitations of this Study

The limitation of this study is that it compares 2 active treatments rather than 1 investigational treatment compared to placebo or usual care. Also, our follow-up was limited to 3 months. Strong points are the randomized study design, the use of 2 rather less investigated treatments which are becoming more common in clinical practice and detailed data collection. To our knowledge, no previous clinical study compared PCN vs. PRF in a randomized controlled trial.

Conclusion

Pain symptoms improve similarly significant in patients with a contained, single-level herniated cervical disk with both PCN and PRF treatment. Although PCN-treated patients reported a trend for faster and more pain improvement compared to PRF, this difference failed to reach statistical significance or a clinically important difference. Other factors (complication risks, duration and treatment costs, burden on the patient, and experience of the treating physician) contribute to the decision to choose 1 treatment over the other.

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Disclosures

The institution W. van der Weegen works for receives study grants from Cotera Inc. and ZimmerBiomet Inc. but these are unrelated to the current study. W. van der Weegen is also a consultant for ZimmerBiomet Inc. None of the others have any disclosures to report.

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Chapter 8

GENERAL DISCUSSION

It is widely accepted that chronic pain reduces quality of life, leads to depression, work absenteeism and inability to participate in activities of daily live. But chronic pain is often not considered as a “stand-alone” disease, and consequently receives less attention from policymakers. As a result, clinical research on chronic pain and its’ treatment are less developed compared to other medical specialities. Hence, I started this thesis project. Chronic pain is not only a medical problem but even more a social problem, imposing a huge burden on society. The costs involved of the medical treatments alone, runs into the hundreds of millions, while the damage in the social field, particularly in the form of absenteeism, amounts to billions of euros and dollars. The International Working Group for chronic pain strongly recommends on improved training and education within all health care curricula[1], and also the need for more and better clinical research on the topic of chronic pain is obvious. Clinical research within pain medicine is an emerging field but considering the importance and impact of chronic pain for both patients and society, there is an important and immediate need for high quality clinical research to relieve this burden by developing and improving chronic pain treatments which are both highly effective, safe and cost-effective, resulting in clear evidence. The aim of this thesis was to analyse the clinical effectiveness and safety of minimal invasive interventional techniques in patients with head and neck pain. First, a retrospective analysis of treatment results was done, followed by prospective and randomized clinical trials. My findings are as follows:

1. The application of pulsed radiofrequency to the atlanto-axial joint is a safe and effective technique in patients with cervicogenic headache (CEH) who are non-responsive to conservative treatment.

I found that pulsed radiofrequency for atlanto-axial joint had a longer duration in efficacy (>50% pain relief at 2 months, 6 months and 1 year) in 50% of all patients at 2 months (43/86), at 6 months (43/86) and in 44.2% of all patients after one year (38/86), compared with intra-articular atlanto-axial steroid injections.[2] Intra-articular injection of steroids is a frequently used procedure, but the duration of the effect of these injections is limited and there may be deleterious side effects if they are repeated too often.[3,4] Also, the potential fatal risk involved with injecting steroids in the atlanto-axial joint should not be underestimated. The atlanto-axial joint may be a possible source of pain in cervicogenic headache but the scientific evidence on applying pulsed radiofrequency to the atlanto-axial joint is scarce. Sluijter et al. published a case report (n=6) using this treatment and reported good results after 1 year.[5] Although the limitation of our study is its’ retrospective design, our data was prospectively collected from ongoing general clinical practice and included a large number of patients (n=86). I concluded that further prospective trials are required to validate our findings and that this technique should be considered earlier in the course of the disease in view of its long-term efficacy. However, this technique should be reserved for highly skilled pain specialists. Further research should focus on improving the diagnostic process, on optimizing CEH patient selection criteria for PRF treatment and on improving technical specifications (i.e. pulse duration, pulse frequency) of PRF treatment for these patients.

2. The application of pulsed radiofrequency of the atlanto-axial joint is a safe and effective technique in patients with whiplash related symptoms.

I retrospectively explored the efficacy of the atlanto-axial joint pulsed radiofrequency treatment in whiplash patients (n=45). Not only the common symptoms in whiplash patients (i.e. headache, neck pain, fatigue) showed a significant improvement but also the cognitive disturbances caused by whiplash such as memory deficit, sleep and concentration disturbances improved. Significantly higher health-related quality of life in terms of bodily pain (p<0.05) and health change (p<0.01) on the SF-36 were observed in our study.[6] A previous study also observed a significant improvement of whiplash related symptoms with PRF treatment of the cervical medial branch only (64.3% of patients with significant pain improvement 9 months after treatment).[7] In our study we compared patient characteristics between responders and non-responders. However, we were unable to detect differences in baseline demographics (i.e. pain before treatment, duration of symptoms) between these two groups. In a more recent study Smith et al. concluded that treating pain in whiplash patients, using conventional neurotomy, was very important for improving the psychological status of these patients[8], which is in concordance with our results. Due to the limiting factors of our retrospective study, pulsed radiofrequency treatment of atlanto-axial joints can only be tentatively viewed as a promising treatment modality for whiplash patients with CEH and should be subject to validation in future prospective studies. Preferably, these studies should use a randomized trial design, comparing pulsed radiofrequency versus standard care and with sufficient follow up duration, preferably one year. One should then also consider using multiple trial arms that include different duration of pulsed radiofrequency treatment.

3. Pulsed radiofrequency treatment of the gasser ganglion is effective in the treatment of specific Trigeminal neuralgia.

In this retrospective study, I explored the effect of percutaneous pulsed radiofrequency treatment of the Ganglion of Gasser in patients with specific trigeminal neuralgia (n=36). All recent patients with typical trigeminal neuralgia from a second level pain center were contacted for a telephonic and medical record evaluation for their current state of pain and the post-procedural data after pulsed radiofrequency treatment of the trigeminal ganglion at 2, 6, and 12 months.[9] In this study all patients received percutaneous pulsed radiofrequency treatment of the gasser ganglion with a duration of 6 to 10 minutes. Most patients experienced excellent pain relief (>80%) at 2, 6, and 12 months (73.5% (25/34), 61.8% (21/34), and 55.9% (19/34)), without complications observed. This result is an encouragement to apply pulsed radiofrequency treatment of the gasser ganglion as an alternative treatment method for trigeminal neuralgia based on: (1) excellent pain relief observed up to one year after treatment; (2) the absence of side effects or complication; (3) pulsed radiofrequency can be used repeatedly without fear for anesthesia dolorosa; (4) pulsed radiofrequency can be also be applied for atypical trigeminal neuralgia, and (5) the first branch of nerve trigeminus can be treated with

pulsed radiofrequency without the effects of corneal lesion. In contrast, some studies showed that pulsed radiofrequency was not effective in trigeminal neuralgia.[10,11] However, these studies used a 2 minutes duration of pulsed radiofrequency rather than 6-10 minutes used in our study. Therefore, further investigations using a prospective study design in specific trigeminal neuralgia patients are recommended to evaluate for better efficacy and evidence by exploring the different stimulation modalities, durations and parameters of pulsed radiofrequency.

4. Percutaneous Cervical Nucleoplasty is a safe and effective treatment in patients with cervical discogenic pain due to a contained disc herniation.

In a retrospective study, I explored the long-term efficacy and safety of PCN, and the influence of optimal selection criteria in a secondary line pain treatment facility. A total of 27 patients treated with PCN fulfilling the selection criteria (Group A) were studied and compared to 42 patients not meeting these specific criteria (Group B). Selection criteria were the number of cervical levels involved, any concomitant cervical spine pathology and possible previous neck surgery. Outcomes were assessed using the Visual Analogue Scale (VAS) and a four-level Likert item for perceived pain and satisfaction, the Neck Disability Index (NDI), and the Short Form 36 (SF-36). Additional relevant clinical outcomes were retrieved from medical records. The following results were observed: The postoperative mean VAS pain for Group A was 29.9 (SD ± 32.6) at a mean follow-up of 24 months (range: 2–45). Only 10% of these patients reported mild transient adverse events. There was a trend, but no significant difference between both groups in pain scores. However, treatment satisfaction was higher for Group A (74.1 ± 27.2–55.5 ± 31.4, P = 0.02). Group A also reported better physical functioning based on the Physical Component Summary (43.6 ± 10.6–37.3 ± 12.0, P = 0.03) and showed a larger proportion of patients no longer using any medication post treatment (63–26%, P = 0.01).[12] Our results are in line with the findings of Li and Yan. Li et al. evaluated the prospective results of 126 PCN procedures for contained cervical disc herniation at 2 weeks, 1, 3, 6 and 12-month follow up. The VAS pain scores improved statistically ($p< 0.01$) for all follow up moments (range 2.42 ±0.71 to 2.44 ± 0.71) compared with pre-treatment findings (7.25 ± 0.44).[14] The rate of excellent and good results based on the modified Macnab criteria was 81.7%. Besides a technical complication (broken device tip) which was of no further consequence, no complications were reported. This study shows PCN to be safe and effective at short-, mid-, and long-term FU. Yan et al. retrospectively compared clinical outcomes of 176 patients with symptomatic contained cervical disc herniation treated with PCN (n = 81) or percutaneous cervical discectomy (PCD) (n=95) at a FU of 16–48 months.[13] In the PCN group, the VAS pain score improved from 7.12 ± 1.13 to 2.74 ± 0.89 ($P < 0.001$) compared with 7.18 ± 1.09 to 2.71 ± 0.91 ($P< 0.001$) in the PCD group. There was no difference found in success rates (Modified Macnab criteria scoring excellent or good) between both groups, respectively, 77.8% (PCN) and 79.5% (PCD). One case of discitis was reported within the PCD group. The results show that both methods are safe and have good long-term clinical

outcomes. This study was of high methodological quality. Hence, overviewing this evidence, percutaneous cervical nucleoplasty (PCN) is a safe and effective treatment in symptomatic patients with contained cervical herniated discs. It provides simple and efficient disc decompression, using a controlled and highly localized ablation, but evidence regarding long-term efficacy is limited. The above presented results show long-term effectiveness and safety of PCN in patients with a one-level contained cervical herniated disc, on the condition that patients are carefully selected, meeting ideal criteria for successful PCN. For the future, these findings must be confirmed in prospective studies including further exploring of multi-level pathology.

5. A systematic review of the literature demonstrated moderate evidence for effectiveness of percutaneous nucleoplasty.

We performed a systematic review of the published literature on cervical nucleoplasty and found that the number of published studies was very low and the quality of the available studies was only moderate.[15] We were able to include 10 articles (3 RCTs and 7 nonrandomized studies) which represented a total of 1021 patients. Of these, 823 patients (≥ 892 discs) were treated by PCN and the remaining patients were controls who were treated with either conservative care or percutaneous cervical discectomy (PCD). All studies showed low methodological quality, except for two. The level of evidence of the RCTs was graded as moderate, with low to moderate applicability and clinical relevance according to these RCTs. This was mainly due to a poorly description of the study population, control intervention, co-interventions, outcome measures, and specific analysis methodologies. Future randomized RCTs on cervical PCN should aim to increase their methodological quality and identify criteria to improve outcome(s).

6. Percutaneous Cervical Nucleoplasty and Pulsed Radiofrequency are equally effective in patients with cervical neck pain.

In a prospective randomized clinical trial, I found that PCN and PRF are equally effective for treating cervical pain caused by a contained single level cervical herniated disc.[16] Cervical neck pain is often caused by cervical disc pathology and hence results in suffering and disability in the adult population. Surgeons as well as patients are increasingly aware of post-surgery-related complications.[17] This stimulated the clinical usage of minimal-invasive treatments such as Percutaneous Nucleoplasty (PCN) and Pulsed Radiofrequency (PRF). However, scientific evidence on both treatments is limited. Therefore, we evaluated the efficacy of PCN compared to PRF in patients with contained cervical disc herniation in a prospective randomized clinical trial including 34 patients with radicular pain due to a single contained cervical disc herniation, treated with either Percutaneous Cervical Nucleoplasty or Pulsed Radio Frequency.[16] Demographic data was collected and patients completed the Medical Outcomes Study 12-Item Short Form (SF-12) Health Survey, visual analog scale (VAS) and the Neck Disability Index

(NDI) 1, 2 and 3 months after treatment. My findings showed that in the Percutaneous Cervical Nucleoplasty group (n=17, mean age 52.4 years, 10 female/7 male) patients were treated at C5-C6 (8 cases) or C6-C7 (9 cases). In the Pulsed Radiofrequency group (n=17, mean age 49.5 years, 8 female/9 male) patients were treated at C3-C4 (1 case), C5-C6 (10 cases) or C6-C7 (6 cases). At three months, mean pain VAS improved significantly from baseline in the Percutaneous Cervical Nucleoplasty group (mean improvement: 43.4 points) and in the Pulsed Radiofrequency group (34.0 points). However, improvement in one group was not superior compared to the other group (p=0.48). No serious complications were reported. Within three months, both PCN and PRF show significant pain improvement in patients with contained cervical disc herniation, but none was superior to the other. Both treatment options appear to be effective and safe in regular clinical practice. Comparing these two interventional techniques towards placebo treatment is not possible in normal clinical practice and research. Further research should focus on optimizing the outcome measures at the long-term for these treatments in patients with difficult to treat cervical neck pain. Strict recommendations on specific selection and inclusion criteria will further improve outcome and limit complications.

General discussion and recommendations

Usually patients with cervical pathology are treated with a variety of conservative treatments (e.g., medication, physiotherapy, manual therapy, epidural injection) which are not very specific, have often low evidence and take a long time to result in a clinical effect including improvement of the quality of life of the individual patient. Surgical treatments, ranging from cervical discectomy to artificial cervical disc replacement are considered if conservative treatments fails but are usually quite invasive with consequently more adjacent risks involved without promising optimal clinical outcome. Minimal invasive pain treatments using percutaneous techniques such as cervical nucleoplasty or pulsed radiofrequency involve, in theory, less risk compared to surgical interventions but hold the promise of being more effective than conservative treatment modalities. Unfortunately the clinical evidence behind minimal invasive pain treatments is still rather limited, and deserves much more attention and research in order to define a more eloquent treatment algorithm for patients with chronic cervical disorders. To build up this evidence, we formulate specific recommendations based on the scientific work presented in this thesis.

Recommendations for clinical practice:

1. Pulsed radiofrequency is equally effective in the treatment of cervical neck pain when applied to the dorsal ganglion in comparison with conventional radiofrequency and therefore should be preferred because of the minimal side effects described.
2. Pulsed radiofrequency treatment is effective in the treatments of upper cervical joint pain (C1-C2) and should be more strongly recommended than intra-articular or per-neural steroid injections.

3. Pulsed radiofrequency is a good alternative for the minimal invasive treatment of trigeminal neuralgia compared to radiofrequency treatment, since it now has been proven to be a safe and effective method for this medical condition.
4. Pulsed radiofrequency can be used repeatedly for patients with different cervical spine pathologies including herniated disc, whiplash associated disorders and trigeminal neuralgia because of the low risk of complications.
5. Pulsed Radiofrequency and Percutaneous Cervical Nucleoplasty both can be used in patients with contained cervical disc herniation since they are equally effective.
6. Percutaneous Cervical Nucleoplasty has on a theoretical basis potentially more risks for complications than pulsed radiofrequency in the treatment of cervical disc hernia.
7. Percutaneous Cervical Nucleoplasty must be applied in a sterile conditions in a fully equipped operation room and can only be performed by a trained and skilled pain specialist who completed this FIPP examination or any other equal accreditation system.

Recommendations for future research:

The impact of chronic pain in quality of life is underestimated and has in all dimensions a worse score than in other chronic conditions. For example, the decrease in quality of life is similar to that of patients with chronic heart failure. Especially in combination with another chronic disease, chronic pain (i.e. back pain, headache) can have a larger than expected negative impact on the self-rated health of the patient. Demyttenaere et al. described that chronic pain patients suffer more from depression, generalized anxiety, agoraphobia or panic disorder, social anxiety disorder, post-traumatic stress, alcoholism and addiction compared to the normal population.[18] These facts combined with the high incidence and prevalence of chronic pain, the wide variety in treatment, and that a relatively large number of patients experienced their treatment for chronic pain as inadequate, signifies the importance of high quality research in this field. Chronic pain not only has a significant impact on quality of life, Activities of Daily Living (ADL), mood, sick leave but is also accompanied by considerable direct and indirect costs. Recent epidemiologic data have shown significant gaps in data and limited quality of published studies. Moreover, specific research methodologies used in pharmacological research are not always possible like blinding and using placebo treatments in minimal invasive and surgical pain treatment techniques. Hence, specific trial adaptations and new research modalities are highly needed to build growing and new evidence in head and neck pain syndromes.

Recommendations for further research:

1. Increase awareness that prospective randomized trials and outcome studies are needed to build further evidence for minimal invasive treatment modalities.
2. Develop clear definitions and a pain classification system to categorize more specifically patient populations that further support research into epidemiology and pathophysiology.

3. Improve knowledge and expertise of pain diagnostics and interventions; include training on chronic pain in the curricula of all medical training courses and develop standards for quality care and outcomes. Epidemiological research helps to raise awareness of these problems and can give direction to future areas of research to improve the pain medicine.
4. Make collaborative initiatives in research between second line pain centers and specific academic research centers to offer optimal high through-put research possibilities in common pain syndromes.
5. Make the need for high quality pain research visible on the national research agenda.

Recommendations for education:

None of the diagnostic tests and minimal invasive interventional techniques should be performed without proper high level specialized training and education, including FIPP examination. Therefore:

1. Increase awareness that good education and training is needed to avoid unwanted effects and complications.
2. Increase general knowledge and expertise about correct diagnosing and treating patients with chronic pain.
3. Educate medical professionals in adequate referring patients with chronic pain to the appropriate medical specialist and treatment program.
4. Medical specialists performing minimal invasive interventional procedures should be highly skilled and trained including an evaluation by e.g. a FIPP examination learning about the evidence, the indications, the limitations, adverse effects and complications of each technique.
5. Educate all medical professionals in standardized quality outcome measures.

In general, nowadays participating in our high demanding modern society has never been more important. The reduced quality of life due to chronic pain is one of the major factors which can people limit to participate fully in our society. This is undesirable and the reason people are looking for solutions. Patients nowadays look further than their known medical specialist and proposed treatments. This is a positive effect and that is why informing our medical colleagues and patients about new medical pain treatments is an important task for us as pain doctors. Due to recent developments in pain practice treatments we have the luxury to have new modern efficient treatments. Especially comparing to older traditional treatments, we can now offer one day pain treatments where patients are able to return home immediately afterwards. This reduces medical costs and allows patients to go to work faster. Post-treatment complications of more invasive treatments can be significantly reduced. The economic benefits are evident, not only the medical cost but also the faster reintegration into the participation of their work. Hence it is important to have clear guidelines and treatment algorithms, not only for medical professionals but also for the patients. This awareness in both groups is important to further exploration new pain treatments. Research and development of the pain field is important for the future and the acceptance of these new pain treatment methods based on the best scientific evidence.

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Chapter 9

SUMMARY

The aim of this thesis research was to investigate the efficacy of pulsed radiofrequency and percutaneous nucleoplasty in patients with chronic pain.

In Chapter 1 we provide an overview of the definition, epidemiology and the impact of chronic pain. The distinction was made between acute and chronic pain and between nociceptive and neuropathic pain, diagnostics and treatment. We discussed the two kinds of treatments (conservative and interventional), each with their risk and benefits.

In Chapter 2 we investigated the efficacy of pulsed radiofrequency treatment in atlanto-axial joint. In this retrospective study, data was collected from one single pain center in ongoing clinical pain practice. We concluded that Pulsed Radiofrequency (PRF) application of the lateral atlanto-axial joint is a feasible and safe technique in patients with cervicogenic headache who are nonresponsive to other techniques, and that it had a longer term efficacy than atlanto-axial intra-articular steroid injection.

In chapter 3 we found that lateral atlanto-axial joint pulsed radiofrequency treatment in whiplash patients with cervicogenic headache improved not only the pain, but also improved cognitive disturbance and fatigue.

In chapter 4 we looked for evidence on pulsed radiofrequency treatment in trigeminal neuralgia. Yes, we found the evidence. We concluded that PRF is also effective in Trigeminal Neuralgia if the duration of the radio frequency takes 6-10 minutes rather than 2 minutes! PRF of the trigeminal ganglion should be further evaluated as an alternative treatment method for Trigeminal Neuralgia.

In chapter 5 we evaluated the long term effectiviness of Percutaneous Cervical Nucleoplasty (PCN) in patients with a one-level contained cervical herniated disk. We also studied the importance of selecting patients meeting ideal criteria for successful PCN. We confirmed in this retrospective study that PCN is effective with long term follow up and also safe to use. Using ideal criteria for successful PCN proved to be important.

In chapter 6 we systematically reviewed current evidence on percutaneous nucleoplasty for cervical herniated disk. All included studies showed PCN to be an effective and safe procedure in the treatment of (contained) herniated disc at short-mid-, and long-term follow-up. However, the level of evidence was moderate and showed only low to moderate applicability and clinical relevance.

In chapter 7 we compared two active methods (percutaneous cervical nucleoplasty versus pulsed radiofrequency of dorsal root ganglion) in treatment of patients with contained cervical disc herniation. After completing this randomized clinical trial we concluded that both PCN and PRF show a significant improvement in pain, but none proved superior to the other. Both treatment options appear to be effective and safe in regular clinical practice.

Chapter 10

NEDERLANDSE SAMENVATTING

Het doel van dit proefschrift was om de werkzaamheid van gepulseerde radiofrequentie en percutane nucleoplasty bij patiënten met chronische pijn te onderzoeken.

In hoofdstuk 1 geven we een overzicht van de definitie, epidemiologie, de impact van chronische pijn, het onderscheid tussen acute en chronische pijn en tussen nociceptieve en neuropathische pijn, diagnostiek en behandeling. We bespraken verder in dit proefschrift de twee soorten van behandeling met hun risico's en voordelen.

In hoofdstuk 2 onderzochten we de effectiviteit van “pulsed radiofrequentie” behandelmethode in het atlanto-axiale gewricht. Dit was een retrospectieve studie en de gegevens werden verzameld uit één pijncentrum. De conclusie van deze studie: Pulsed radiofrequentie therapie (PRF) met een laterale atlanto-axiale benadering van het atlanto-axiale (AA) gewricht is een haalbare en veilige techniek bij patiënten met cervicogene hoofdpijn die niet responsief zijn voor andere technieken en deze therapie heeft een langere termijn werkzaamheid dan atlanto-axiale intra-articulaire steroïde injectie.

In hoofdstuk 3 vonden we dat pulsed radiofrequentie therapie met een laterale atlanto-axiale benadering van het AA gewricht in whiplash patiënten met cervicogene hoofdpijn niet alleen de pijn verbeterde, maar ook de cognitieve stoornis en vermoeidheid.

In hoofdstuk 4 in dit proefschrift onderzochten we de effectiviteit van PRF bij trigeminusneuralgie. Ja, we vonden het bewijs. Het percentage van de patiënten die een uitstekende verlichting van de pijn (> 80% pijnverlichting) toonden na 2, 6 en 12 maanden was 73.5% (25/34), 61.8% (21/34) en 55.9 % (19/34) respectievelijk. Het percentage patiënten met voldoende pijnverlichting (50-80% pijnverlichting) na 2, 6 en 12 maanden bedroeg 14.7% (5/34), 17.6% (6/34) en 17.6% (6/34) respectievelijk. Er werden geen complicaties fo heropnames gerapporteerd. Conclusies: PRF is ook effectief in Trigeminusneuralgie wanneer de duur van de radiofrequentie 6-10 minuten bedraagt! PRF van het trigeminale ganglion moet verder worden geëvalueerd als een alternatieve werkwijze voor trigeminusneuralgie behandeling.

In hoofdstuk 5 onderzoeken we Percutane cervicale Nucleoplasty (PCN), de meest toegepaste techniek op het cervicale niveau met een laag risico op thermische schade. Verschillende gepubliceerde studies hebben aangetoond dat PCN veilig en effectief is. Hoewel deze behandelings-modaliteit is beschreven in de literatuur, was het beschikbare bewijs over de werkzaamheid niet voldoende om definitieve conclusies over de optimale therapie te maken. We bevestigden in deze retrospectieve studie de lange termijn effectiviteit en veiligheid van PCN bij patiënten met een cervicale hernia op één niveau. Daarnaast toonden we aan dat strikte selectie van patiënten aan de hand van duidelijke criteria tot een meer succesvolle PCN behandeling leid.

In hoofdstuk 6 voerden we een systematische review uit van de huidige literatuur van percutane nucleoplasty als behandeling voor cervicale hernia. Alle geïncludeerde studies toonden aan dat PCN een effectieve en veilige procedure is voor de behandeling van cervicale hernia op korte, middellange en lange termijn follow-up. De bewijskracht is matig en toont slechts geringe tot matige toepasbaarheid en klinische relevantie.

In hoofdstuk 7 vergelijken we twee actieve therapieën: PCN versus PRF van de dorsale wortel ganglion bij patiënten met cervicale hernia. Het bewijs voor de effectiviteit van deze interventies, PCN en PRF van dorsale wortel ganglion is nog niet goed gedocumenteerd bij patiënten met cervicale hernia. We concluderen dat zowel PCN als PRF tot een significante verbetering van de pijnklachten leid bij patiënten met een cervicale hernia, maar geen van beide is superieur. Beide behandelingen lijken effectief en veilig in de reguliere klinische praktijk. Er is behoefte aan meer hoogwaardige RCT onderzoek met gebruik van gevalideerde uitkomstmaten naar de werkzaamheid en veiligheid van beide technieken. Bovendien moet de gezondheids-economische waarde met betrekking tot deze behandelingen van cervicale discogene pijn worden geanalyseerd.

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About the author

Willy Halim who's name at birth is 'Lim Soey Giap' was born in Jakarta on December 27th, 1949. After one year study at the Medical Faculty of the University of Kristen Indonesia (UKI) in Jakarta he continued his medical study at the Catholic University of Leuven (KUL), Belgium. He went back to Indonesia after his medical study in 1977 to help his father in law as director of a farmaceutical company (Saka Farma, Semarang) for two years (1978-1980). In 1978 he also passed the Examination for the Medical Part of ECFMG (Educational Commission For Medical Graduates). A tragic event with his first wife, who died after giving birth to a daughter in Semarang, made him return to the medical world. After post graduate training in anesthesiology at the Onze Lieve Vrouw Clinic (Aalst, Belgium), he worked as an anesthesiologist in the Zuiderzee Hospital (Lelystad, the Netherlands) untill March 1987. From April 1987 to March 2006 he worked in the Vlietland hospital, Schiedam. From 1988 onwards he specialized in Pain Therapy under supervison of Dr. Michael Sanders at the Spaarne Hospital, Haarlem. From 1992 to 1996 he was a senior lecturer in Pain Therapy at the Erasmus Medisch Centrum, Rotterdam and in March 2007 he became a Fellow of Interventional Pain Practise (FIPP). Since March 2006 he worked as a pain therapy practictioner at the St.Anna hospital in Geldrop, from which he retired at the end of 2016. Currently he lives in Nuenen and is happily married to Florence Adam with whom he has two sons, Stanley and Jonathan. He still frequently visits Indonesia to lecture at national and local scientific meetings.